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Requester's Full Name: Maher Haddad Examiner #: 79112 Date: 6/17/03
Art Unit: 1644 Phone Number 306-3472 Serial Number: 10/019,437
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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

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Jan,

- Please search claims 1-3, 5, 7 and 10
- Please search SEQ ID NO: 1+2 (close + open)

Thanks
Maher

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Date Completed: <u>6/29/03</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems <u>✓</u>
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Online Time: <u>60</u>	Other _____	Other (specify) _____

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L1 3 S (L-CITRULLINE OR D-CITRULLINE OR DL-CITRULLINE)/CN
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E SSERRE G/AU
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L2 45 S E3,E4,E5
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L3 21 S E3,E4
L4 47 S L2,L3
E FIBRIN/CT
E E3+ALL
L5 842 S E1
E E2+ALL
L6 6094 S E5
L7 17163 S FIBRIN
E E8+ALL
L8 15852 S E6,E5+NT
E FIBRINOGEN
L9 28056 S E3
L10 2 S L4 AND L5-L9
L11 3400 S L1
L12 6856 S CITRUL?
L13 12 S L11,L12 AND L4
L14 2 S L13 AND L10
L15 11 S (?RHEUMAT? OR ?ARTHRIT?) AND L13,L14
L16 2 S L14 AND L15
L17 10 S L10,L13-L15 NOT L16
L18 2 S L5-L7 AND L11
L19 5 S L5-L7 AND L12
L20 9 S L8,L9 AND L11,L12
L21 9 S L18-L20
L22 4 S (?RHEUMAT? OR ?ARTHRIT?) AND L21
L23 4 S L16,L22
L24 1 S L18,L19 NOT L23
L25 4 S L21 NOT L22-L24
SEL DN AN 4
L26 1 S L25 AND E1-E3
L27 5 S L23,L26

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FILE COVERS 1907 - 29 Jun 2003 VOL 139 ISS 1
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This file contains CAS Registry Numbers for easy and accurate
substance identification.

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L27 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2003:472715 HCAPLUS

TI Method of detecting autoantibodies from patients suffering from
rheumatoid arthritis, a peptide and an assay kit

IN Van Venrooij, Waltherus Jacobus Wilhelmus; Drijfhout, Jan Wouter; Van
Boekel, Martinus Adrianus Maria; Pruijn, Gerardus Jozef Maria

PA Stichting Voor De Technische Wetenschappen, Neth.

SO PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N033-564

ICS G01N033-68; C07K007-08; C07K014-47

CC 15 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003050542	A2	20030619	WO 2002-NL815	20021211
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI NL 2001-1019540 A 20011211

AB The invention relates to method of detecting autoantibodies from patients suffering from **rheumatoid arthritis**. To this end, according to the invention, at least two peptide units are used of which at least one peptide unit comprises a part not derived from (pro)collagen, **fibrin**, **fibrinogen**, vimentin, cytokeratin 1 and cytokeratin 9, and which peptide unit comprises the motif XG, and a peptide unit comprising the motif XnonG, wherein X is a **citrullin** or an analogue thereof, and nonG is an amino acid other than glycine.

L27 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:927627 HCAPLUS

DN 138:23681

TI Marker genes for the diagnosis, molecular definition and development of treatment of chronic inflammatory joint diseases using microarray technologies

IN Haeupl, Thomas; Ungethuem, Ute; Blaess, Stefan

PA Pathoarray GmbH, Germany

SO PCT Int. Appl., 56 pp.

CODEN: PIXXD2

DT Patent

LA German

IC ICM C12Q001-68

CC 15-8 (Immunochemistry)

Section cross-reference(s): 3

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	WO 2002097125	A2	20021205	WO 2002-DE2010	20020530
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10127572	A1	20021205	DE 2001-10127572	20010530
	DE 10225853	A1	20030515	DE 2002-10225853	20020530
PRAI	DE 2001-10127572	A	20010530		
AB	The invention relates to tools for the diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases and other inflammatory, infectious or tumorous diseases. According to the invention, genome data (genomics), proteome data (proteomics) and immunome data (immunomics) are used in the anal. and development of treatment of chronic joint diseases. Anal. of patterns of gene expression at the mRNA or protein level and of the distribution of antigens are used to characterize inflammatory and non-inflammatory rheumatic joint diseases, auto-immune diseases and infectious diseases and in the identification of diagnostic indicators. Etiol. significant pathogenic factors in chronic inflammatory joint diseases which have been unclear until now can be derived from the exams. carried out. Furthermore, interpretation algorithms can be created for the classification, prognosis evaluation and treatment optimization of said joint diseases, and new strategies for treatment and points of attack for medicaments can be derived.				
ST	microarray analysis protein mRNA inflammatory autoimmune disease diagnosis; osteoarthritis diagnosis microarray transcriptome proteome immunome; rheumatoid arthritis diagnosis microarray transcriptome proteome immunome				
IT	Villin RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (2, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)				
IT	Antigens RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (CH65 (chondrocyte antigen 65), as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)				
IT	Chaperonins RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (DnaJ, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)				
IT	Antigens RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (EBNA1 (Epstein-Barr virus-assocd. nuclear antigen 1), as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)				

- IT Immunoglobulins
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (G, .gamma.-chain, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (GRP78 (glucose-regulated protein, 78 kDa), as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Heat-shock proteins
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (HSP 47, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Heat-shock proteins
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (HSP 60, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Antigens
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (SA, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (YKL-39 (chondrocyte protein 39), as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteome
 RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
 (anal. of in diagnosis of inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Protein microarray technology
 (antibody; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Aggreccans
 Calreticulin
 Fibrinogens
 Fibrins
 Filaggrin
 Moesins
 Radixin
 Rheumatoid factors
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Antibodies
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL

- (Biological study); USES (Uses)
(autoantibodies, diagnostic detection of; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Immunity
(autoimmunity, in **rheumatoid arthritis**, diagnostic anal. of; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT T cell (lymphocyte)
(autoreactive, diagnostic detection of; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cartilage link protein, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Peptides, biological studies
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**citrulline**-contg., as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(collagen-binding, colligin 2, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT PCR (polymerase chain reaction)
(diagnostic, high throughput; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Joint, anatomical
(disease, inflammation, chronic; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Gene
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(expression, in autoimmune disease, therapeutic modulation of; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Glycoproteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gp39, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(hnRNPA2, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Autoimmune disease
Blood analysis
DNA microarray technology

High throughput screening

Osteoarthritis

Protein microarray technology

Rheumatoid arthritis

(marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)

- IT Diagnosis
(mol.; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Data processing
(of microarray data in diagnosis of autoimmune disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Proteins
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(synovial stimulatory protein P205, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT Collagens, biological studies
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(type XI, as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)
- IT 9024-52-6, Fructose bisphosphate aldolase 79079-11-1, Calpastatin 188364-80-9, Matrix metalloproteinase MMP19
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(as diagnostic marker for inflammatory disease; marker genes for diagnosis, mol. definition and development of treatment of chronic inflammatory joint diseases using microarray technologies)

L27 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:205541 HCAPLUS

DN 134:352031

TI The major synovial targets of the **rheumatoid arthritis** -specific antifilaggrin autoantibodies are deiminated forms of the .alpha.- and .beta.-chains of **fibrin**

AU Masson-Bessiere, Christine; **Sebbag, Mireille**; Girbal-Neuhausser, Elisabeth; Nogueira, Leonor; Vincent, Christian; Senshu, Tatsuo; **Serre, Guy**

CS Department of Biology and Pathology of the Cells, Institut National de la Sante et de la Recherche Medicale Contrat Jeune Formation 96-02, Toulouse-Purpan School of Medicine, University Toulouse III (Institut Federatif de Recherche 30, Institut National de la Sante et de la Recherche Medicale-Centre, Toulouse, Fr.

SO Journal of Immunology (2001), 166(6), 4177-4184
CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

CC 15-2 (Immunochemistry)

AB IgG anti-filaggrin autoantibodies (AFA) are the most specific serol. markers of **rheumatoid arthritis**. In epithelial tissues, they recognize **citrulline**-bearing epitopes present on various mol. forms of (pro)filaggrin. Histol. anal. of **rheumatoid** synovial membranes with an Ab to **citrulline** showed labeling of interstitial amorphous deposits and mononuclear cells of various types. Immunochem. anal. of exhaustive sequential exts. of the same tissues

showed that they contain several deiminated (**citrulline** contg.) proteins. Among them, two proteins, p64-78 and p55-61, present in urea-DTT and guanidine exts., were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identified as deiminated forms of the .alpha.- and .beta.-chains of **fibrin**, resp. Their identity was confirmed using several Abs specific for the A.alpha.- and/or to the B.beta.-chain of **fibrin** (ogen). Moreover, AFA-pos. **rheumatoid arthritis** (RA) sera and purified AFA were highly reactive to the A.alpha.- and B.beta.-chains of human **fibrinogen** only after deimination of the mols. by a peptidylarginine deiminase. Autoantibodies affinity purified from a pool of RA sera onto deiminated **fibrinogen** were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated A.alpha.-and B.beta.-chains of **fibrinogen**, the autoantibodies to the synovial proteins p64-78 and p55-61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of **fibrin** deposited in the **rheumatoid** synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated **fibrin** is a crit. step in RA pathogenesis.

ST **arthritis** filaggrin autoantibody **fibrin**

IT Antibodies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(autoantibodies; .alpha.- and .beta.-chains of **fibrin** are targets of anti-filaggrin antibodies in **rheumatoid arthritis**)

IT **Rheumatoid arthritis**

(.alpha.- and .beta.-chains of **fibrin** are targets of anti-filaggrin antibodies in)

IT **Fibrinogens**

Fibrins

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(.alpha.- and .beta.-chains of **fibrin** are targets of anti-filaggrin antibodies in **rheumatoid arthritis**)

IT Filaggrin

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(.alpha.- and .beta.-chains of **fibrin** are targets of anti-filaggrin antibodies in **rheumatoid arthritis**)

IT 75536-80-0, Peptidylarginine deiminase

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(deimination of **fibrinogen** generates reactivity for **rheumatoid** anti-filaggrin antibodies)

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L27 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:31538 HCAPLUS

DN 134:95494

TI **Citrulline-containing fibrin derivatives, and their use for diagnosing or treating rheumatoid arthritis**

IN **Serre, Guy; Sebbag, Mireille**

PA Universite Paul Sabatier - Toulouse III, Fr.

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM C07K014-75

ICS A61K038-36; A61P019-02; G01N033-53

CC 1-7 (Pharmacology)

Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001002437	A1	20010111	WO 2000-FR1857	20000630
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2795735	A1	20010105	FR 1999-8470	19990701
	FR 2795735	B1	20010907		
	EP 1196450	A1	20020417	EP 2000-949595	20000630
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2003504314	T2	20030204	JP 2001-508224	20000630

PRAI FR 1999-8470 A 19990701
WO 2000-FR1857 W 20000630.

AB The invention provides **citrulline**-contg. polypeptides which are derived from **fibrin** and are useful for diagnosing or treating **rheumatoid arthritis**.

ST **fibrin citrulline** deriv **rheumatoid arthritis** treatment; diagnosis **rheumatoid arthritis fibrin citrulline** deriv

IT **Fibrinogens**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(and deiminated **fibrinogen**; **citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT Filaggrin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(autoantibodies to; **citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT Antibodies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(autoantibodies; **citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT **Antirheumatic agents**
Immunoassay
Rheumatoid arthritis
Test kits
(**citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT **Fibrins**
Proteins, general, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT Proteins, specific or class
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with carrier mols.; **citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT Animal tissue
(synovial; **citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT **372-75-8, Citrulline**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(**citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

IT 2489-13-6 47295-77-2 99235-09-3 318500-71-9 318500-76-4 318500-81-1
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(**citrulline**-contg. **fibrin** derivs., and use for diagnosing or treating **rheumatoid arthritis**)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Scripps Research Inst; WO 9528946 A 1995 HCAPLUS

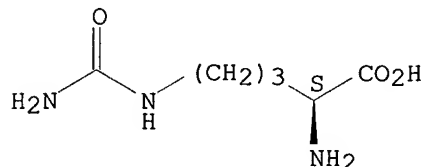
IT **372-75-8, Citrulline**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
 BIOL (Biological study); OCCU (Occurrence)
 (citrulline-contg. fibrin derivs., and use for
 diagnosing or treating rheumatoid arthritis)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2003 ACS

AN 2000:349085 HCAPLUS

DN 133:9150

TI Stabilized protein preparation for a tissue adhesive

IN Metzner, Hubert; Gronski, Peter

PA Centeon Pharma G.m.b.H., Germany

SO Ger. Offen., 18 pp.

CODEN: GWXXBX

DT Patent

LA German

IC ICM A61L024-00

ICS A61K038-36

CC 63-7 (Pharmaceuticals)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19853033	A1	20000525	DE 1998-19853033	19981118
	EP 1131110	A1	20010912	EP 1999-972113	19991116
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002529202	T2	20020910	JP 2000-582086	19991116
	US 6447774	B1	20020910	US 2001-856195	20010713
PRAI	DE 1998-19853033	A	19981118		
	WO 1999-EP8812	W	19991116		
AB	Stabilized, essentially fibrinogen -free protein preps. storable in the liq. state are described which contain a factor XIII conc., a salt of an org. di- or tricarboxylic acid, (esp. of citric acid), and other usual stabilizers for factor XIII preps. Stabilized frozen fibrinogen preps. are also described which contain fibrinogen aggregation-inhibiting chaotropic agents and remain stable for >4 wk after thawing. The factor XIII and fibrinogen preps. can be used after mixing, along with a thrombin prepn., as a tissue adhesive. The stabilized prepn. also preferably contains an antifibrinolytic agent such as aprotinin or lysine. A kit contains stabilized factor XIII, stabilized fibrinogen , and a thrombin-contg. soln. packaged sep. from each other. The prepn. can be refrozen after thawing without loss of activity, in case not all of the prepn. is used for a given application. At <10.degree. the shelf-life of the prepn. is .gtoreq.1 yr.				
ST	tissue adhesive factor XIII stabilization; coagulation factor XIII stabilization adhesive; fibrinogen stabilization tissue adhesive				
IT	Freezing				
	(-thawing; stabilized protein prepn. for tissue adhesive)				
IT	Adhesives				
	(biol.; stabilized protein prepn. for tissue adhesive)				

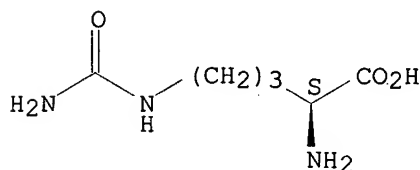
- IT Denaturants
(chaotropic; stabilized protein prepn. for tissue adhesive)
- IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dicarboxylic, salts; stabilized protein prepn. for tissue adhesive)
- IT Fibrinolysis
(inhibitors; stabilized protein prepn. for tissue adhesive)
- IT Denaturation
(protein, inhibitors of; stabilized protein prepn. for tissue adhesive)
- IT Stabilizing agents
(stabilized protein prepn. for tissue adhesive)
- IT **Fibrinogens**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilized protein prepn. for tissue adhesive)
- IT Alditols
Amino acids, biological studies
Disaccharides
Monosaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized protein prepn. for tissue adhesive)
- IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tricarboxylic acids, salts; stabilized protein prepn. for tissue adhesive)
- IT 9013-56-3, Blood-coagulation factor XIII
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stabilized protein prepn. for tissue adhesive)
- IT 9002-04-4, Thrombin 9087-70-1, Aprotinin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized protein prepn. for tissue adhesive)
- IT 50-21-5D, Lactic acid, salts 52-90-4, L-Cysteine, biological studies
56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 56-84-8D, L-Aspartic acid, salts, biological studies 56-85-9, L-Glutamine, biological studies 56-86-0D, L-Glutamic acid, salts, biological studies 56-87-1, L-Lysine, biological studies 56-91-7, p-Aminomethylbenzoic acid 57-13-6, Urea, biological studies 57-50-1, Sucrose, biological studies 60-32-2, .epsilon.-Aminocaproic acid 68-04-2, Trisodium citrate 69-65-8, D-Mannitol 71-00-1, L-Histidine, biological studies 74-79-3, L-Arginine, biological studies 77-92-9D, Citric acid, salts 98-92-0, Nicotinamide 113-00-8, Guanidine 372-75-8, L-Citrulline 556-50-3, Glycylglycine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized protein prepn. for tissue adhesive)
- RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
- RE
- (1) Anon; EP 0487713 B1 HCAPLUS
(2) Anon; EP 0592242 A1 HCAPLUS
(3) Anon; EP 0855667 A1
(4) Anon; EP 0856317 A1 HCAPLUS
(5) Anon; DE 19617369 A1 HCAPLUS
(6) Anon; DE 3734923 C1 HCAPLUS
(7) Anon; DE 69121528 T2
- IT 372-75-8, L-Citrulline

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized protein prepn. for tissue adhesive)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d 117 all hitstr tot

L17 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2003:106795 HCAPLUS

DN 138:332584

TI cDNA cloning, gene organization and expression analysis of human
peptidylarginine deiminase type I

AU Guerrin, Marina; Ishigami, Akihito; Mechin, Marie-Claire; Nachat, Rachida;
Valmary, Severine; **Sebbag, Mireille**; Simon, Michel; Senshu,
Tatsuo; **Serre, Guy**

CS INSERM U563 - P. Sabatier University (IFR30, INSERM-CNRS-P. Sabatier
Universite-Centre Hospitalier Universitaire), Department of Epidermal
Differentiation and Rheumatoid Autoimmunity, Toulouse-Purpan
Pathophysiology Center, Toulouse, 31073, Fr.

SO Biochemical Journal (2003), 370(1), 167-174

CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.

DT Journal

LA English

CC 3-3 (Biochemical Genetics)

Section cross-reference(s): 7, 13

AB Peptidylarginine deiminases (PADs) catalyze a post-translational
modification of proteins through the conversion of arginine residues into
citrullines. The existence of four isoforms of PAD (types I, II,
III and IV) encoded by four different genes, which are distinct in their
substrate specificities and tissue-specific expression, was reported in
rodents. In the present study, starting from epidermis polyadenylated
RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding
human PAD type I. The cDNA was 2711 bp in length and encoded a
663-amino-acid sequence. The predicted protein shares 75% identity with
the rat PAD type I sequence, but displays only 50-57% identity with the
three other known human isoforms. We have described the organization of
the human PAD type I gene on chromosome 1p36. A recombinant PAD type I
was produced in *Escherichia coli* and shown to be enzymically active.
Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only
in the epidermis, but also in various organs, including prostate, testis,
placenta, spleen and thymus. In human epidermis exts. analyzed by Western
blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement
with its predicted mol. mass. As shown by immunohistochem., the enzyme
was expressed in all the living layers of human epidermis, with the
labeling being increased in the granular layer. This is the first
description of the human PAD type I gene and the first demonstration of
its expression in epidermis.

ST human peptidylarginine deiminase type I cDNA sequence; chromosome mapping
human PAD gene evolution

IT Gene, animal

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (PAD type I; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)

- IT Genetic mapping
 - Human
 - Placenta
 - Prostate gland
 - Protein sequences
 - Spleen
 - Testis
 - Thymus gland
 - cDNA sequences
 - (cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT Skin
 - (epidermis, granular layer; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT Chromosome
 - (human 1, 1p36, PAD type I gene maps to; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT Evolution
 - (mol.; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT 481136-05-4P
 - RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
 - (amino acid sequence; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT 75536-80-0, Peptidylarginine deiminase
 - RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 - (cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)
- IT 245373-33-5
 - RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 - (nucleotide sequence; cDNA cloning, gene organization and expression anal. of human peptidylarginine deiminase type I)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L17 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:964626 HCAPLUS

DN 138:38086

TI Filaggrin and **citrulline**-containing filaggrin and the diagnostic detection of autoantibodies in **rheumatoid arthritis**

IN Incauragarat, Brigitte; Jolivet, Michel; Letourneur, Odile; Nogueira, Maria Leonor; **Sebbag, Mireille; Serre, Guy; Vincent, Christian**

PA Biomerieux, Fr.

SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM G01N033-564

ICS G01N033-68

CC 15-8 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002101390	A2	20021219	WO 2002-FR2032	20020613
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	FR 2826124	A1	20021220	FR 2001-8068	20010613
PRAI	FR 2001-8068	A	20010613		

AB The invention concerns a method for detecting **rheumatoid arthritis**-specific autoantibodies in a biol. sample. The method involves measuring the immunopptn. of filaggrin or filaggrin fragments and the corresponding fragments in which there is partial substitution of

arginine by **citrulline** by a sample thought to contain antibodies. The ratio of the two values is indicative of autoantibodies to filaggrin and can be used as a diagnostic indicator. Rat filaggrin was prep'd. by expression of the cloned gene. The protein was then **citrullinated** with peptidyl arginine deiminase to give 53% conversion of arginine to **citrulline**. The pptn. of the proteins was tested using antiserum from patients suffering any of several different autoimmune diseases. Only antiserum from **polyrheumatoid arthritis** patients pptd. the filaggrins.

ST filaggrin **citrulline** autoantibody **rheumatoid arthritis** diagnosis

IT Antibodies

RL: ANT (Analyte); ANST (Analytical study)
(autoantibodies, to filaggrin, diagnostic detection of; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT Filaggrin

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**citrulline**-contg.; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT Human

Immunoassay

Rheumatoid arthritis

(filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT Filaggrin

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT Protein sequences

(for filaggrin of rat; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT Diagnosis

(immunodiagnosis, of **rheumatoid arthritis**;
filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 250686-73-8 250686-74-9 478550-27-5 478550-28-6

RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence, filaggrin fragment; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 478585-38-5P

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 478585-39-6

RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 75536-80-0, Protein arginine deiminase

RL: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)

(in **citrullination** of autoantigens; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 74-79-3, L-Arginine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (substitution by **citrulline** of, in autoantigens; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

IT 372-75-8, L-Citrulline

RL: BSU (Biological study, unclassified); BIOL (Biological study) (substitution of arginine by, in autoantigens; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

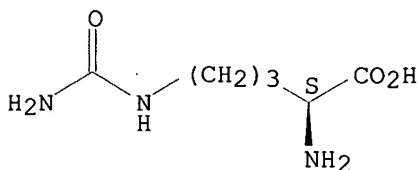
IT 372-75-8, L-Citrulline

RL: BSU (Biological study, unclassified); BIOL (Biological study) (substitution of arginine by, in autoantigens; filaggrin and **citrulline**-contg. filaggrin and diagnostic detection of autoantibodies in **rheumatoid arthritis**)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:697965 HCAPLUS

DN 137:383509

TI Detection of antibodies to deiminated recombinant rat filaggrin by enzyme-linked immunosorbent assay: a highly effective test for the diagnosis of **rheumatoid arthritis**

AU Vincent, Christian; Nogueira, Leonor; **Sebbag, Mireille**; Chapuy-Regaud, Sabine; Arnaud, Michel; Letourneur, Odile; Rolland, Dominique; Fournie, Bernard; Cantagrel, Alain; Jolivet, Michel; **Serre, Guy**

CS Institut National de la Sante et de la Recherche Medicale (CJF 96-02, IFR30), Purpan School of Medicine, University of Toulouse III, Toulouse, Fr.

SO Arthritis & Rheumatism (2002), 46(8), 2051-2058

CODEN: ARHEAW; ISSN: 0004-3591

PB John Wiley & Sons, Inc.

DT Journal

LA English

CC 15-1 (Immunochemistry)

AB Objective. To assay antifilaggrin autoantibodies, we developed an ELISA using a "**citrullinated**" recombinant rat filaggrin. Our objectives were to assess its value for diagnosing **rheumatoid arthritis** (RA) and to compare the results with those obtained using 4 other ref. methods for detection of antifilaggrin autoantibodies, including the com. available ELISA that uses a modified "**citrullinated**" synthetic peptide derived from the sequence of human filaggrin (CCP-ELISA). Methods. We analyzed 711 sera from patients with well-characterized **rheumatic** diseases, including 240 patients with RA. Antifilaggrin autoantibodies were detected by an ELISA

using a recombinant rat filaggrin deiminated in vitro as immunosorbent (ArFA-ELISA). The results considered were the differences between the optical densities obtained on deiminated and nondeiminated proteins. Antibodies to rat esophagus epithelium were detected by indirect immunofluorescence, while antibodies to human filaggrin were detected by immunoblotting and by a recently described ELISA using a deiminated recombinant human filaggrin. Finally, CCP-ELISA was performed according to the manufacturer's recommendations. Results. At the titer thresholds allowing diagnostic specificities of 0.95, 0.985, and 0.99 to be reached, the diagnostic sensitivities of the ArFA-ELISA were 0.76, 0.67, and 0.65, resp. At these 3 thresholds, the sensitivities were significantly higher than those of the 4 other tests. Despite incomplete overlapping of the 5 tests, the high diagnostic performance of the ArFA-ELISA allows us to propose this test to replace all the other methods for antifilaggrin autoantibody detection. Conclusion. ArFA-ELISA appears to be the most efficient test among those available for the detection of antifilaggrin autoantibodies, in terms of diagnostic accuracy for RA. Its diagnostic performance in early RA and its prognostic value are currently under evaluation.

ST autoantibody filaggrin **rheumatoid arthritis** diagnosis

IT Antibodies

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(autoantibodies; detection of antibodies to deiminated recombinant rat filaggrin by ELISA in diagnosis of **rheumatoid arthritis**)

IT Filaggrin

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(deiminated; detection of antibodies to deiminated recombinant rat filaggrin by ELISA in diagnosis of **rheumatoid arthritis**)

IT Blood analysis

Human

Rheumatoid arthritis

(detection of antibodies to deiminated recombinant rat filaggrin by ELISA in diagnosis of **rheumatoid arthritis**)

IT Filaggrin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(detection of antibodies to deiminated recombinant rat filaggrin by ELISA in diagnosis of **rheumatoid arthritis**)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L17 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:448386 HCAPLUS

DN 137:261500

TI Identification of **citrullinated rheumatoid**

arthritis-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay

AU Union, Ann; Meheus, Lydie; Humbel, Rene Louis; Conrad, Karsten; Steiner, Guenter; Moereels, Henri; Pottel, Hans; **Serre, Guy**; De Keyser, Filip

CS Innogenetics NV, Ghent, 9052, Belg.

SO Arthritis & Rheumatism (2002), 46(5), 1185-1195

CODEN: ARHEAW; ISSN: 0004-3591

PB John Wiley & Sons, Inc.

DT Journal

LA English

CC 15-1 (Immunochemistry)

AB Objective: To identify immunodominant epitopes in natural filaggrin that are reactive with antifilaggrin autoantibodies (AFA) in the sera of patients with **rheumatoid arthritis** (RA) and to explore their use in a diagnostic assay format. Based on the results of epitope mapping of human natural filaggrin as well as mol. modeling and computational chem., synthetic peptides together with recombinant **citrullinated** filaggrin were evaluated by a line immunoassay (LIA) for AFA detection. Diagnostic performance was assessed using 336 RA and 253 disease control sera and was compared with that of ref. methods. Several immunoreactive epitopes were identified in natural filaggrin, all of which contained at least 1 **citrulline** residue. Three antigenic substrates, including 2 synthetic peptides and recombinant **citrullinated** filaggrin showing maximal reactivity on LIA, were finally selected. Using the 3-antigen LIA3, overall sensitivity, specificity, and pos. predictive value for RA were 65.2%, 98.0%, and 89.1%, resp., compared with 61.9%, 98.8%, and 92.8% using the 2-antigen LIA2 (without recombinant protein). Thirty-seven percent of the **rheumatoid** factor (RF)-neg. RA samples (30 of 81) were AFA-pos. by LIA2, and 52 of 54 RF-pos. control samples had no AFA detected on LIA2. Higher specificity and sensitivity were obtained by LIA2 vs. anti-RA33 immunoblot, whereas good agreement was obsd. with antikeratin antibody testing. LIA performed significantly better than AFA immunoblotting using natural filaggrin, at a specificity level of 99% (P = 0.0047). **Citrullinated** residues are present in immunoreactive epitopes of natural human filaggrin. AFA can be readily detected by **citrullinated** peptides in an LIA-based test, resulting in high specificity and pos. predictive value for RA. The LIA could serve as a user-friendly alternative to existing immunofluorescence tests and AFA immunoblot techniques. Given its complementarity to RF, this test can be a valuable tool in the differential diagnosis of **arthritis**.

ST immunoassay diagnosis autoantibody **rheumatoid arthritis**
filaggrin diagnosis

IT Antibodies

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL

- (Biological study); USES (Uses)
 (autoantibodies; identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT Peptides, biological studies
 RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (**citrulline**-contg.; identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT Blood analysis
 Epitopes
 Human
 Immunoassay
Rheumatoid arthritis
 (identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT **Rheumatoid factors**
 RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT Filaggrin
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT Diagnosis
 (serodiagnosis; identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT 462082-86-6 462082-88-8 462082-90-2 462082-92-4 462082-94-6
 RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)
- IT **372-75-8, Citrulline**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (identification of **citrullinated rheumatoid arthritis**-specific epitopes in natural filaggrin relevant for antifilaggrin autoantibody detection by line immunoassay)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
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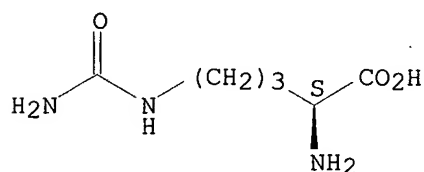
IT 372-75-8, **Citrulline**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (identification of **citrullinated rheumatoid**
arthritis-specific epitopes in natural filaggrin relevant for
 antifilaggrin autoantibody detection by line immunoassay)

RN 372-75-8. HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2002:1017 HCAPLUS

DN 136:384829

TI Specific presence of intracellular **citrullinated** proteins in
rheumatoid arthritis synovium: Relevance to
 antifilaggrin autoantibodies

AU Baeten, Dominique; Peene, Isabelle; Union, Ann; Meheus, Lydie;
Sebbag, Mireille; Serre, Guy; Veys, Eric M.; De Keyser,
 Filip

CS Ghent University, Ghent, Belg.

SO Arthritis & Rheumatism (2001), 44(10), 2255-2262

CODEN: ARHEAW; ISSN: 0004-3591

PB Wiley-Liss, Inc.

DT Journal

LA English.

CC 15-8 (Immunochemistry)

AB To investigate the presence of **citrullinated** proteins in the synovial membrane of patients with **rheumatoid arthritis** (RA) and controls, and to analyze a possible relationship with antifilaggrin auto-antibody (AFA) reactivity. Synovial biopsy samples were obtained from 88 consecutive patients undergoing needle arthroscopy for knee synovitis assocd. with RA (n = 36), spondylarthropathy (n = 35), **osteoarthritis** (n = 9), or other diagnoses (n = 8). Tissue sections were stained with 2 different anticitrulline polyclonal antibodies and an antifilaggrin monoclonal antibody (mAb). The phenotype of **citrulline**-pos. cells and the colocalization with affinity-purified AFA were investigated by double immunofluorescence on frozen sections. Studies with the first antibody showed that **citrulline** is expressed intracellularly in the lining and sublining layers of RA synovial tissue. Staining with the second antibody, monospecific for proteins contg. modified **citrulline**, and with anti-inducible nitric oxide synthetase confirmed the presence of **citrullinated** proteins rather than free **citrulline** in the synovium. **Citrulline**-pos. cells were detected in 50% of the RA patients (18 of 36) but in none of the controls (0 of 52). The anticitrulline reactivity colocalized with affinity-purified AFA reactivity, although stainings with the antifilaggrin mAb indicated the absence of filaggrin in the synovium. Intracellular **citrullinated** proteins, which are not recognized by an antifilaggrin mAb, are expressed in RA but not in control synovium. The high specificity of this finding and the colocalization with AFA reactivity boost the interest in **citrullinated** proteins as possible triggers of autoimmune responses in RA. Moreover, this is the first description of a specific histol. marker for RA synovium.

ST human **rheumatoid arthritis citrullinated**
protein synovium antifilaggrin autoantibody

IT Antibodies

RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(autoantibodies; intracellular **citrullinated** proteins in **rheumatoid arthritis** synovium relevance to antifilaggrin autoantibodies)

IT Biomarkers (biological responses)

Human

Rheumatoid arthritis

Synovial membrane

(intracellular **citrullinated** proteins in **rheumatoid arthritis** synovium relevance to antifilaggrin autoantibodies)

IT Proteins

RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(intracellular **citrullinated** proteins in **rheumatoid arthritis** synovium relevance to antifilaggrin autoantibodies)

IT 372-75-8, **Citrulline**

RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(intracellular **citrullinated** proteins in **rheumatoid arthritis** synovium relevance to antifilaggrin autoantibodies)

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IT 372-75-8, **Citrulline**

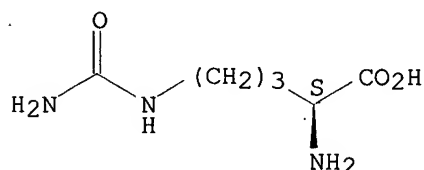
RL: ADV (Adverse effect, including toxicity); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(intracellular **citrullinated** proteins in **rheumatoid arthritis** synovium relevance to antifilaggrin autoantibodies)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 2001:689574 HCAPLUS

DN 136:277638

TI Performance of two ELISAs for antifilaggrin autoantibodies, using either affinity purified or deiminated recombinant human filaggrin, in the diagnosis of **rheumatoid arthritis**

AU Nogueira, L.; **Sebbag, M.**; Vincent, C.; Arnaud, M.; Fournie, B.; Cantagrel, A.; Jolivet, M.; **Serre, G.**

CS Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale, Preval, Fr.

SO Annals of the Rheumatic Diseases (2001), 60(9), 882-887

CODEN: ARDIAO; ISSN: 0003-4967

PB BMJ Publishing Group

DT Journal

LA English

CC 15-1 (Immunochemistry)

AB Objective-To develop a standardizable enzyme linked immunosorbent assay (ELISA), using human filaggrin, for detection of antifilaggrin autoantibodies in **rheumatoid arthritis** (RA). To compare the diagnostic performance of the ELISA with those of ref. tests: "anti-keratin antibodies" ("ANA"), and antibodies to human epidermis filaggrin detected by immunoblotting (Alfa-IB). Methods-Two ELISAs were

developed using either affinity purified neutralacidic human epidermis filaggrin (AhFA-ELISA-pur) or a recombinant human filaggrin deiminated in vitro (AhFA-ELISA-rec) as immunosorbent. Antifilaggrin autoantibodies were assayed in 714 serum samples from patients with well characterized **rheumatic** diseases, including 241 RA and 473 other **rheumatic** diseases, using the two ELISAs. "AKA" and AhFA-IB tests were carried out in the same series of patients. The diagnostic performance of the four tests was compared and their relationships analyzed. Results-The titers of "AKA", AhFA-IB, and the AhFA-ELISAs correlated strongly with each other. The diagnostic sensitivity of the AhFA-ELISA-rec, which was better than that of AhFA-ELISA-pur, was 0.52 for a specificity of 0.95. This performance was similar to those of "AKA" or AhFA-IB. However, combining AhFA-ELISA-rec with AhFA-IB led to a diagnostic sensitivity of 0.55 for a specificity of 0.99. Conclusion-A simple and easily standardizable ELISA for detection of antifilaggrin autoantibodies was developed and validated on a large series of patients using a **citrullinated** recombinant human filaggrin. The diagnostic performance of the test was similar to that of the "AKA" and AhFA-IB. Nevertheless, combining the AhFA-ELISA-rec with one of the other tests clearly enhanced the performance.

ST ELISA filaggrin autoantibody immunodiagnosis **rheumatoid arthritis**

IT Human

Rheumatoid arthritis

(ELISAs for antifilaggrin autoantibodies, using human filaggrin, in diagnosis of **rheumatoid arthritis**)

IT Filaggrin

Keratins

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)

(ELISAs for antifilaggrin autoantibodies, using human filaggrin, in diagnosis of **rheumatoid arthritis**)

IT Antibodies

RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(autoantibodies; ELISAs for antifilaggrin autoantibodies, using human filaggrin, in diagnosis of **rheumatoid arthritis**)

IT Immunoassay

(enzyme-linked immunosorbent assay; ELISAs for antifilaggrin autoantibodies, using human filaggrin, in diagnosis of **rheumatoid arthritis**)

IT Diagnosis

(immunodiagnosis; ELISAs for antifilaggrin autoantibodies, using human filaggrin, in diagnosis of **rheumatoid arthritis**)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L17 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:785829 HCAPLUS

DN 132:11629

TI Peptide epitopes recognized by antifilaggrin auto-antibodies present in serum of **rheumatoid arthritis** patients and their use in diagnosis

IN **Serre, Guy Bruno Rene**; Girbal Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; **Sebbag, Mireille**; Dalbon, Pascal; Jolivet Reynaud, Colette; Arnaud, Michel; Jolivet, Michel

PA Bio Merieux S. A., Fr.

SO Fr. Demande, 21 pp.

CODEN: FRXXBL

DT Patent

LA French

IC ICM C07K014-47

ICS A61K038-17; G01N033-564

CC 15-2 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2773157	A1	19990702	FR 1997-16673	19971230
	FR 2773157	B1	20011005		
	CA 2316269	AA	19990715	CA 1998-2316269	19981229
	WO 9935167	A1	19990715	WO 1998-FR2899	19981229
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	AU 9919717	A1	19990726	AU 1999-19717	19981229
	EP 1042366	A1	20001011	EP 1998-964536	19981229
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		

PRAI FR 1997-16673 A 19971230

WO 1998-FR2899 W 19981229

AB **Citrulline**-contg. peptides recognized by autoantibodies from the serum of patients with **rheumatoid arthritis** are disclosed. These peptides may be used in immunoassays for detection of these autoantibodies and for diagnosis of this disease. Thus, expts. showed that **citrulline**-contg. peptide 71-119 of human filaggrin reacted with the autoantibodies of **rheumatoid arthritis** patients while the same peptide, in which the arginine residue had not been converted to **citrulline** by the action of peptidyl arginine deiminase, did not react. Two 14-amino acid **citrulline**-contg. peptides which also are recognized by these autoantibodies were prepd.

ST **rheumatoid arthritis** diagnosis immunoassay

autoantibody filaggrin epitope **citrulline**

IT Antibodies

RL: ANT (Analyte); ANST (Analytical study)
 (autoantibodies; peptide epitopes recognized by antifilaggrin
 auto-antibodies present in serum of **rheumatoid**
arthritis patients and their use in diagnosis)

IT Epitopes

Immunoassay

Rheumatoid arthritis

(peptide epitopes recognized by antifilaggrin auto-antibodies present
 in serum of **rheumatoid arthritis** patients and their
 use in diagnosis)

IT Filaggrin

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(peptide epitopes recognized by antifilaggrin auto-antibodies present
 in serum of **rheumatoid arthritis** patients and their
 use in diagnosis)

IT 204391-63-9 204391-64-0

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(peptide epitopes recognized by antifilaggrin auto-antibodies present
 in serum of **rheumatoid arthritis** patients and their
 use in diagnosis)

IT 251365-12-5

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)

(residues 71-119 of human filaggrin; peptide epitopes recognized by
 antifilaggrin auto-antibodies present in serum of **rheumatoid**
arthritis patients and their use in diagnosis)

IT 225682-08-6, GenBank A69712 225682-09-7, GenBank A69713

RL: PRP (Properties)

(unclaimed nucleotide sequence; peptide epitopes recognized by
 antifilaggrin auto-antibodies present in serum of **rheumatoid**
arthritis patients and their use in diagnosis)

IT 250722-30-6

RL: PRP (Properties)

(unclaimed protein sequence; peptide epitopes recognized by
 antifilaggrin auto-antibodies present in serum of **rheumatoid**
arthritis patients and their use in diagnosis)

L17 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:785823 HCAPLUS

DN 132:444

TI Use of filaggrin-derived **citrulline**-containing peptides for
 treatment of **rheumatoid polyarthritis**

IN **Serre, Guy Bruno Rene**; Girbal Neuhauser, Elisabeth; Vincent,
 Christian; **Sebbag, Mireille**; Simon, Michel; Dalbon, Pascal;
 Jolivet Reynaud, Colette; Arnaud, Michel; Jolivet, Michel

PA Universite Paul Sabatier Toulouse III, Fr.

SO Fr. Demande, 25 pp.

CODEN: FRXXBL

DT Patent

LA French

IC ICM A61K038-17

CC 1-7 (Pharmacology)

Section cross-reference(s): 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2773078	A1	19990702	FR 1997-16672	19971230
	FR 2773078	B1	20000526		
	CA 2315294	AA	19990715	CA 1998-2315294	19981229
	WO 9934819	A2	19990715	WO 1998-FR2900	19981229
	WO 9934819	A3	19991104		

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID,
 IL, IN, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX,

NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZW,
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9919718 A1 19990726 AU 1999-19718 19981229
 EP 1041997 A2 20001011 EP 1998-964537 19981229
 EP 1041997 B1 20030416

R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI
 JP 2002500195 T2 20020108 JP 2000-527267 19981229
 AT 237345 E 20030515 AT 1998-964537 19981229

PRAI FR 1997-16672 A 19971230
 WO 1998-FR2900 W 19981229

AB Antigenic peptides derived from filaggrin, and in which at least one arginine residue has been replaced by a **citrulline** residue, are used for the prepn. of medicaments for the treatment of **rheumatoid polyarthritis**.

ST **citrulline** contg filaggrin peptide **rheumatoid polyarthritis**

IT Antibodies

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(autoantibodies, to filaggrin; filaggrin-derived **citrulline** -contg. peptides for treatment of **rheumatoid polyarthritis**)

IT **Antirheumatic agents**

(filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT Filaggrin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT Lymphocyte

(plasma cell, synovial; filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT **372-75-8, Citrulline**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(arginine replacement by; filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT **74-79-3, L-Arginine, biological studies**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**citrulline** replacement for; filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT 250686-73-8D, arginine-to-**citrulline** replacement derivs.

250686-74-9D, arginine-to-**citrulline** replacement derivs.

251102-69-9D, arginine-to-**citrulline** replacement derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(filaggrin-derived **citrulline**-contg. peptides for treatment of **rheumatoid polyarthritis**)

IT 250686-75-0

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); OCCU (Occurrence)
(filaggrin-derived **citrulline**-contg. peptides for treatment
of **rheumatoid polyarthritis**)

IT 372-75-8, **Citrulline**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)

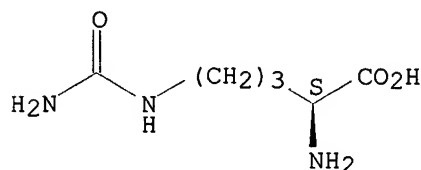
(arginine replacement by; filaggrin-derived **citrulline**-contg.

peptides for treatment of **rheumatoid polyarthritis**)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1999:33223 HCAPLUS

DN 130:195491

TI The epitopes targeted by the **rheumatoid arthritis**

-associated antifilaggrin autoantibodies are posttranslationally generated
on various sites of (pro)filaggrin by deimination of arginine residues

AU Girbal-Neuhauser, Elisabeth; Durieux, Jean-Jacques; Arnaud, Michel;

Dalbon, Pascal; **Sebbag, Mireille**; Vincent, Christian; Simon,

Michel; Senshu, Tatsuo; Masson-Bessiere, Christine; Jolivet-Reynaud,

Colette; Jolivet, Michel; **Serre, Guy**

CS Department of Biology and Pathology of the Cell, Institut National de la
Sante et de la Recherche Medicalet, Toulouse-Purpan School of Medicine,
University Toulouse III, Toulouse, Fr.

SO Journal of Immunology (1999), 162(1), 585-594

CODEN: JOIMA3; ISSN: 0022-1767

PB American Association of Immunologists

DT Journal

LA English

CC 15-2 (Immunochemistry)

AB Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies
assocd. to **rheumatoid arthritis** (RA), which includes
the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the
most specific serol. markers of RA. We previously showed that they
recognize human epidermal filaggrin and other profilaggrin-related
proteins of various epithelial tissues. Here, we report further
characterization of the protein Ags and epitopes targeted by AFA. All the
Ags that exhibit numerous neutral/acidic isoelec. variants were
immunochem. demonstrated to be deiminated proteins. In vitro deimination
of a recombinant human filaggrin by a peptidylarginine deiminase generated
AFA epitopes on the protein. Moreover, two of three filaggrin-derived
synthetic peptides with a **citrulline** in the central position
were specifically and widely recognized by AFA affinity-purified from a
series of RA sera. These results indicate that **citrulline**
residues are constitutive of the AFA epitopes, but only in the context of
specific amino acid sequences of filaggrin. In competition expts., the
two peptides abolished the AFA reactivity of RA sera, showing that they
present major AFA epitopes. These data should help in the identification
of a putative deiminated AFA-inducing or cross-reactive articular
autoantigen and provide new insights into the pathogenesis of RA. They
could also open the way toward specific immunosuppressive and/or
preventive therapy of RA.

ST **rheumatoid arthritis** filaggrin peptide deimination
autoantibody

IT Immunoglobulins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(autoantibodies, G; epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT Imination
(de-; epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT Epithelium
Epitopes
Post-translational processing
Rheumatoid arthritis
(epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT Filaggrin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT Filaggrin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(profilaggrins; epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT 75536-80-0, Peptidylarginine deiminase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT 74-79-3, L-Arginine, biological studies 372-75-8, L-Citrulline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

IT 204391-63-9 204391-64-0
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(epitopes targeted by **rheumatoid arthritis**-assocd. antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
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IT 372-75-8, L-Citrulline

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

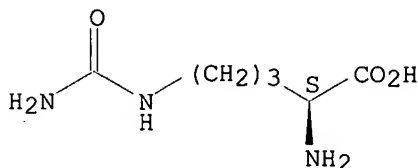
(epitopes targeted by **rheumatoid arthritis**-assocd.

antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues)

RN 372-75-8 HCAPLUS

CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L17 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS

AN 1998:163682 HCAPLUS

DN 128:229350

TI **Citrulline**-containing antigens derived from filaggrin and their use for diagnosing **rheumatoid polyarthritis**

IN **Serre, Guy**; Girbal-Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; **Sebbag, Mireille**; Dalbon, Pascal;

Jolivet-Reynaud, Colette; Arnaud, Michel; Jolivet, Michel

PA Biomerieux, Fr.; Serre, Guy; Girbal-Neuhauser, Elisabeth; Vincent, Christian; Simon, Michel; Sebbag, Mireille; Dalbon, Pascal;

Jolivet-Reynaud, Colette; Arnaud, Michel; Jolivet, Michel

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM C12N015-12

ICS C12N001-21; C07K014-47; C12N009-78; G01N033-53

CC 15-2 (Immunochemistry)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9808946	A1	19980305	WO 1997-FR1541	19970901
	W: CA, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2752842	A1	19980306	FR 1996-10651	19960830
	FR 2752842	B1	19981106		
	EP 929669	A1	19990721	EP 1997-938965	19970901
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	FR 1996-10651		19960830		
	WO 1997-FR1541		19970901		
AB	The invention concerns an artificial antigen specifically identified by the anti-filaggrin autoantibodies present in the serum of patients suffering from rheumatoid polyarthritis , and consisting of one polypeptide comprising all or part of the sequence of one filaggrin unit or of a related mol., in which an arginine residue has been substituted by a citrulline residue. The invention also concerns the use of this antigen for diagnosing rheumatoid polyarthritis . Peptides corresponding to human filaggrin residues 71-119 as well as tetradecapeptides EQSADSSRHSGSGH and ESSRDGSRHPRSHD were synthesized and treated with peptidyl arginine deiminase to convert the arginyl residues to citrullinyl residues. These peptides reacted with sera from patients suffering from rheumatoid polyarthritis .				
ST	filaggrin citrulline diagnosis rheumatoid polyarthritis				
IT	Antigens				
	RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (artificial; citrulline -contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis)				
IT	Antibodies				
	RL: ANT (Analyte); ANST (Analytical study) (autoantibodies, to filaggrin; citrulline -contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis)				
IT	Diagnosis				
	Rheumatoid arthritis (citrulline -contg. antigens derived from filaggrin and their use for diagnosing rheumatoid polyarthritis)				
IT	Filaggrin				
	RL: BSU (Biological study, unclassified); BIOL (Biological study)				

(citrulline-contg. antigens derived from filaggrin and their use for diagnosing **rheumatoid polyarthrititis**)

IT 204391-63-9P 204391-64-0P 204594-23-0P
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
 (citrulline-contg. antigens derived from filaggrin and their use for diagnosing **rheumatoid polyarthrititis**)

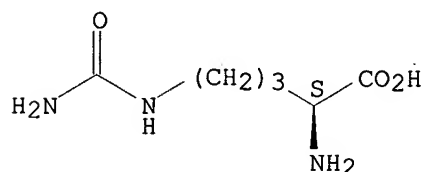
IT 372-75-8, **Citrulline**
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (citrulline-contg. antigens derived from filaggrin and their use for diagnosing **rheumatoid polyarthrititis**)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
 (1) Clonatec; WO 9219649 A 1992 HCAPLUS
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IT 372-75-8, **Citrulline**
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
 (citrulline-contg. antigens derived from filaggrin and their use for diagnosing **rheumatoid polyarthrititis**)

RN 372-75-8 HCAPLUS
 CN L-Ornithine, N5-(aminocarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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 FILE 'WPIX' ENTERED AT 10:37:57 ON 29 JUN 2003
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FILE LAST UPDATED: 24 JUN 2003 <20030624/UP>
 MOST RECENT DERWENT UPDATE: 200340 <200340/DW>
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L55 ANSWER 1 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 2003-148833 [14] WPIX

DNN N2003-117453

TI Detecting auto-antibodies specific for rheumatoid polyarthritis, useful for diagnosis, based on their differential reaction with native and **citrullinated** filaggrin.

DC S03

IN INCAURGARAT, B; JOLIVET, M; LETOURNEUR, O; NOGUEIRA, M L; **SEBBAG, M**; SERRE, O; VINCENT, C; **SERRE, G**

PA (INMR) BIO MERIEUX; (INMR) BIOMERIEUX SA

CYC 100

PI WO 2002101390 A2 20021219 (200314)* FR 24p G01N033-564

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
ZW

FR 2826124 A1 20021220 (200315) G01N033-543

ADT WO 2002101390 A2 WO 2002-FR2032 20020613; FR 2826124 A1 FR 2001-8068
20010613

PRAI FR 2001-8068 20010613

IC ICM G01N033-543; G01N033-564

ICS G01N033-68

AB WO2002101390 A UPAB: 20030227

NOVELTY - Method for detecting autoantibodies (A) specific for rheumatoid polyarthritis (RP) in a sample that may also contain antibodies not specific for RP.

DETAILED DESCRIPTION - Method for detecting autoantibodies (A) specific for rheumatoid polyarthritis (RP) in a sample that may also contain antibodies not specific for RP comprises first reacting the sample with (i) filaggrin or its derivative or a related peptide containing at least one Arg residue (collectively FNC) and (ii) **citrullinated** filaggrin, or its derived peptide (collectively PFC), so that immune complexes are formed with (A). Complexes formed between (i) FNC or PFC and (ii) (A) or other antibodies are detected and quantified as Xnc and Xc, respectively, then Xnc is subtracted from Xc.

USE - For diagnosis of rheumatoid polyarthritis.

ADVANTAGE - Compared with known methods, the process has greater specificity while retaining high sensitivity.

Dwg.0/0

FS EPI

FA AB

MC EPI: S03-E14H; S03-E14H4

TECH UPTX: 20030227

TECHNOLOGY FOCUS - BIOLOGY - Preferred Materials: FNC is the human or rat protein, particularly recombinant rat protein of 399 amino acids (sequence reproduced) or any of 5 specified peptides. PFC is formed from FNC by the action of peptidyl arginine deiminase and at least 20, best 50, % of Arg residues are **citrullinated**, i.e. have the amidino group replaced by aminocarbonyl. The test sample is blood, plasma or serum. Preferred Process: The immune complexes formed are reacted with a conjugate comprising a labeled antibody (lAb) directed against human immunoglobulin (Ig) and the labeled complex formed is detected and quantified.

Particularly lAb contains alkaline phosphatase or peroxidase, and detection is by colorimetry or fluorimetry, with Xnc and Xc expressed as optical or fluorescent densities. Where Xc is greater than Xnc, presence of RP-specific autoantibodies is indicated. Preferably FNC and PFC are immobilized on solid supports and the test is performed like an enzyme-linked immunosorbent assay.

ABEX

UPTX: 20030227

EXAMPLE - A microtiter plate was coated with recombinant rat filaggrin, then blocked and incubated for 1 hour at 37degreesC with a 1:100 dilution of test serum in pH 7.6 buffer. The plates were washed, incubated with a labeled anti-human immunoglobulin G, washed again, color developed from o-phenylenediamine (10 minutes at 18-25degreesC), then optical density measured at 492 nm, to give a value FNC. A second test was performed similarly using a plate coated with **citrullinated** filaggrin to give a value FC. For 63 control samples the value of FC-FNC was in the range -0.445 to +0.731, with 60 of them negative, but for 65 samples from patients with rheumatoid polyarthritis FC-FNC was in the range -0.343 to +2.944 (17 were negative; one was zero and the others were positive. The threshold value for 99% specificity was 0.65, compare 0.4 to 0.5 for known tests, indicating the greater reliability of the assay.

L55 ANSWER 2 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 2002-068306 [10] WPIX

DNN N2002-050576 DNC C2002-020581

TI Reducing or inhibiting post-operative tissue adhesions using tissue adhesive, comprises stabilized **fibrinogen** preparation containing chaotropic agent, and thrombin preparation,.

DC B04 B05 D16 D22 P34

IN DICKNEITE, G; KROEZ, M; METZNER, H

PA (AVET) AVENTIS BEHRING GMBH; (CENT-N) CENTEON PHARMA GMBH

CYC 31

PI EP 1157706 A2 20011128 (200210)* DE 8p A61L024-10

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

AU 2001046166 A 20011129 (200210) A61L024-00

CA 2348119 A1 20011122 (200210) EN A61L024-10

DE 10025001 A1 20011129 (200210) A61L024-00

JP 2001327592 A 20011127 (200210) 6p A61L024-00

US 2002001584 A1 20020103 (200210) A61L024-00

KR 2001107601 A 20011207 (200236) A61L024-00

ADT EP 1157706 A2 EP 2001-111013 20010508; AU 2001046166 A AU 2001-46166
20010521; CA 2348119 A1 CA 2001-2348119 20010517; DE 10025001 A1 DE
2000-10025001 20000522; JP 2001327592 A JP 2001-150784 20010521; US
2002001584 A1 US 2001-861657 20010522; KR 2001107601 A KR 2001-27633
20010521

PRAI DE 2000-10025001 20000522

IC ICM A61L024-00; A61L024-10

ICS A61K038-48; A61L033-00

AB EP 1157706 A UPAB: 20020213

NOVELTY - The use of a tissue adhesive (I) is claimed for reducing or inhibiting post-operative tissue adhesions, where (I) comprises: (a) a stabilized **fibrinogen** preparation, which is storable in a liquid and/or frozen state and contains a chaotropic agent; and (b) a thrombin preparation.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of a tissue adhesive comprising (a) a stabilized **fibrinogen** preparation, which is storable in a liquid and/or frozen state and (b) a thrombin preparation, where the **fibrinogen** component (a) has a reduced plasminogen content.

ACTIVITY - Antiadhesive; Hemostatic.

MECHANISM OF ACTION - None given in the source material.

USE - For reducing or inhibiting post-operative tissue adhesions.

ADVANTAGE - (I) has a superior antiadhesive effect to prior art

tissue adhesives, while retaining good hemostatic activity.

Dwg.0/0

FS CPI GMPI

FA AB; DCN

MC CPI: B04-D01; B04-H19; B05-A01B; B05-C07; B07-D09; B10-A07; B10-A13C;
B10-A17; B10-B02A; B10-B02D; B10-B02J; B10-C02; B10-C04D; B14-F02;
B14-F08; B14-N14; D09-C04B

TECH UPTX: 20020213

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (I) optionally further includes a preparation (c) containing blood coagulation Factor XIII (which may be mixed with (a)) and/or an **antifibrinolytic** agent (specifically epsilon-aminocaproic acid, p-aminobenzoic acid and/or aprotinin). The preparation of the **fibrinogen** component (a) includes additional purification stages; preferably (a) has a reduced plasminogen content, especially such that the weight ratio of plasminogen to **fibrinogen** is less than 0.00018 : 1. The Factor XIII preparation (c) preferably contains a salt of a di-, tri- or tetracarboxylic acid and optionally further stabilizer(s) (specifically one or more of mono- or disaccharides, sugar alcohols, the aminoacids glycine, glycylglycine, alanine, cysteine, histidine or glutamine, salts or glutamine or aspartic acid, reducing agents, antioxidants or surfactants). The **fibrinogen** component (a) contains one or more of arginine, guanidine, **citrulline**, urea or their derivatives as chaotropic agent; and optionally further contains stabilizer(s) selected from inorganic salts, carboxylic acid salts (especially citrates or lactates), aminoacids, mono- or disaccharides or sugar alcohols. The thrombin preparation (b) is stable in the liquid and/or frozen state, and contains (in addition to a calcium salt and sodium chloride) stabilizer(s) selected from buffers, sugars, sugar alcohols, aminoacids and/or salts of mono- or polycarboxylic acids. (b) specifically contains a non-covalent bonding inhibitor as stabilizer. (b) is purified by hydrophobic interaction chromatography (optionally together with cation exchange chromatography).

Viruses in (I) (or its components) are inactivated or removed.

ABEX UPTX: 20020213

EXAMPLE - A tissue adhesive (Ia) was prepared from: (a) a **fibrinogen** component comprising 90 mg/ml **fibrinogen** concentrate, 100 mM sodium chloride, 20 mM trisodium citrate dihydrate, 237 mM arginine hydrochloride and 80 mM epsilon-aminocaproic acid (or 1000 KIU aprotinin); (b) a thrombin component comprising 1500 IU/ml thrombin concentrate, 150 mM sodium chloride, 40 mM calcium chloride, 110 mM mannitol and 5 mM L-histidine; and (c) a Factor XIII component comprising 120 U/ml Factor XIII concentrate, 10 mM trisodium citrate dihydrate and 50 mM L-histidine. The pH of (Ia) after mixing was 7.4. When tested in a rabbit uterine horn adhesion model, application of (Ia) to the wounds reduced the frequency of adhesions (determined 7 days later) from 63.6% (in untreated controls) to 11.1%.

L55 ANSWER 3 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 2001-114394 [13] WPIX

DNN N2001-084087 DNC C2001-034134

TI New **citrulline**-containing polypeptide from **fibrin**,
useful for diagnosis and treatment of rheumatoid polyarthritis.

DC B04 D16 S03

IN SEBBAG, M; SERRE, G

PA (UYTO-N) UNIV TOULOUSE SABATIER PAUL

CYC 22

PI FR 2795735 A1 20010105 (200113)* 23p C07K014-745 <--

WO 2001002437 A1 20010111 (200113) FR C07K014-75 <--

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: CA JP US

EP 1196450 A1 20020417 (200233) FR C07K014-75 <--

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

JP 2003504314 W 20030204 (200320) 23p C07K014-75 <--
 ADT FR 2795735 A1 FR 1999-8470 19990701; WO 2001002437 A1 WO 2000-FR1857
 20000630; EP 1196450 A1 EP 2000-949595 20000630, WO 2000-FR1857 20000630;
 JP 2003504314 W WO 2000-FR1857 20000630, JP 2001-508224 20000630
 FDT EP 1196450 A1 Based on WO 200102437; JP 2003504314 W Based on WO 200102437
 PRAI FR 1999-8470 19990701
 IC ICM **C07K014-745; C07K014-75**
 ICS A61K038-00; **A61K038-36; A61P019-02;**
A61P029-00; A61P037-00; G01N033-53; G01N033-68
 AB FR 2795735 A UPAB: 20010307

NOVELTY - **Citrulline (Cit)** containing polypeptide (I)
 derived from all or part of the alpha - or beta -chains of **fibrin**
 (from a vertebrate) by substitution of at least one arginine residue by
Cit, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:

(1) antigenic composition for detecting autoantibodies (AAb) specific
 for rheumatoid polyarthritis (RP), comprising at least one (I), optionally
 labeled and/or conjugated to a carrier protein;

(2) method for detecting AAb;

(3) kit for detecting AAb; and

(4) pharmaceutical composition containing at least one (I) as active
 ingredient.

ACTIVITY - Anti-arthritis; anti-inflammatory.

No biological data is given.

MECHANISM OF ACTION - Neutralization of an autoimmune response,
 especially inhibition of fixation of humoral/cellular effectors of the
 response. The antigen responsible for the autoimmune response in
 rheumatoid polyarthritis has been identified as **citrulline**
 -containing derivatives of **fibrin** chains.

USE - (I) are used for in vitro diagnosis of rheumatoid polyarthritis
 (RP), by detecting disease-specific autoantibodies, and therapeutically
 for neutralizing the RP-associated autoimmune response.

ADVANTAGE - (I) can detect autoantibodies associated with rheumatoid
 polyarthritis in serum with high sensitivity.

Dwg.0/3

FS CPI EPI

FA AB; DCN

MC CPI: B04-G01; B04-N0200E; B11-C07A; B12-K04; **B14-C06;**

B14-C09B; D05-H07; D05-H09; D05-H11

EPI: S03-E14H

TECH UPTX: 20010307

TECHNOLOGY FOCUS - BIOLOGY - Preferred Polypeptide: (I) contains at least
 5, particularly at least 10, consecutive amino acids from the
fibrin chains, especially from a mammalian, specifically human,
fibrin.

Preferred Method: To detect AAb, a test sample is incubated with (I) and
 any AAb-antigen complexes formed are detected conventionally.

Preferred Kits: The kits contain at least one (I) plus standard buffers
 and reagents for forming and detecting an immune complex.

Preparation: (I) may be obtained from **fibrin** or
fibrinogen (natural, recombinant or synthetic), or
 arginine-containing fragments, by treatment with peptidyl arginine
 deiminase.

Preferred Process: Proteins were extracted from synovial tissues,
 separated by electrophoresis and tested for reaction with anti-filigrin
 auto-antibodies (AAF). Two proteins (64-78 and 55-61 kDa) were recognized
 in urea/dithiothreitol extracts from patients with RP. Partial sequencing
 of these proteins show them to be encoded by the genes for the alpha and
 beta-**fibrin** chain precursors. Further analysis showed that AAF
 are not significantly reactive with the normal **fibrinogen** chains
 but react strongly with those chains that have been deiminated in vivo to
 convert arginine to **Cit**.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) may be produced by usual methods of peptide synthesis, with direct incorporation of **Cit** during synthesis. Synthetic (I) may be pseudopeptides with retro or retro-inverso residues (to increase resistance to proteases).

ABEX UPTX: 20010307

ADMINISTRATION - (I) are administered orally, parenterally or locally. No dose is suggested.

L55 ANSWER 4 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 2000-377495 [33] WPIX

DNN N2000-283436 DNC C2000-114403

TI Stabilized factor XIII and **fibrinogen** preparations useful as tissue adhesive components.

DC B04 D16.D22 P34

IN GRONSKI, P; METZNER, H

PA (CENT-N) CENTEON PHARMA GMBH; (AVET) AVENTIS BEHRING GMBH

CYC 86

PI DE 19853033 A1 20000525 (200033)* 18p A61L024-00

WO 2000029041 A1 20000525 (200033) DE A61L024-10

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
UA UG US UZ VN YU ZW

AU 2000013834 A 20000605 (200042) A61L024-10

EP 1131110 A1 20010912 (200155) DE A61L024-10

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

KR 2001101028 A 20011114 (200230) A61L024-10

US 6447774 B1 20020910 (200263) A61K038-48

JP 2002529202 W 20020910 (200274) 33p A61L024-00

ADT DE 19853033 A1 DE 1998-19853033 19981118; WO 2000029041 A1 WO 1999-EP8812 19991116; AU 2000013834 A AU 2000-13834 19991116; EP 1131110 A1 EP 1999-972113 19991116; WO 1999-EP8812 19991116; KR 2001101028 A KR 2001-706252 20010517; US 6447774 B1 WO 1999-EP8812 19991116, US 2001-856195 20010713; JP 2002529202 W WO 1999-EP8812 19991116, JP 2000-582086 19991116

FDT DE 19853033 A1 Div in DE 19861158; AU 2000013834 A Based on WO 200029041; EP 1131110 A1 Based on WO 200029041; US 6447774 B1 Based on WO 200029041; JP 2002529202 W Based on WO 200029041

PRAI DE 1998-19853033 19981118

IC ICM A61K038-48; A61L024-00; A61L024-10

ICS A61K035-14; A61K038-00; **A61K038-36**; C07K017-00

AB DE 19853033 A UPAB: 20000712

NOVELTY - A **fibrinogen**-free, factor XIII preparation is stabilized with a di- or tricarboxylic acid salt and other stabilizers. Also new are **fibrinogen**-containing preparations stabilized with chaotropic substances and a tissue adhesive pack consisting of the factor XIII preparation, a **fibrinogen**-containing preparation and a thrombin preparation.

DETAILED DESCRIPTION - A stabilized, **fibrinogen**-free, protein preparation which can be stored in liquid form contains:

- (a) blood coagulation factor XIII;
- (b) a di- or tricarboxylic acid salt, especially a citrate; and
- (c) additional factor XIII stabilizers.

INDEPENDENT CLAIMS are also included for:

- (A) a stabilized, liquid or deep-frozen protein preparation containing **fibrinogen** and less than 0.28 mol/l of a chaotropic substance which prevents or reduces **fibrinogen** aggregation; and
- (B) a tissue adhesive comprising a unit pack containing as separate components either:

- (i) the stabilized **fibrinogen**-free protein preparation, the

stabilized, liquid or deep-frozen, **fibrinogen**-containing protein preparation and a thrombin-containing preparation; or

(ii) a mixture of the **fibrinogen**-free and **fibrinogen**-containing protein preparations and a thrombin-containing preparation.

USE - As tissue adhesive or for topical and parenteral therapeutic treatment.

ADVANTAGE - Compared with prior art formulations known from e.g. EP85923, DE19617369, EP856317 and 487713, the preparations have improved stability without loss of activity of the active agent and/or a reduced content of chaotropic substances. E.g., after a deep frozen preparation has been thawed it has a shelf life of at least 4 weeks up to several months compared with a few days for conventional concentrates.

Dwg.0/0 .

FS CPI GMPI

FA AB; DCN

MC CPI: B04-H19; B07-A02; B07-D04C; B07-D09; B10-A07; B10-A13C; B10-A13D; B10-A17; B10-B02D; B10-B02J; B10-C02; B10-C04D; B12-M06; B14-N17B; D05-A02C; D09-A01

TECH UPTX: 20000712

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Preparations: The stabilized, **fibrinogen**-free preparation contains a mono- or disaccharide or a sugar alcohol and/or glycine, glycyglycine, alanine, cysteine, histidine, aspartic acid, glutamine or a glutamine salt as the additional stabilizer (c). The stabilized, liquid or deep-frozen **fibrinogen**-containing preparation contains arginine, guanidine, urea, **citrullin** and/or nicotinamide as the chaotropic substance. It can also contain an antifibrotic comprising aprotinin, lysine, p-aminocaproic acid, p-aminomethylbenzoic acid or salt or derivative as an antifibrotic and a stabilizer comprising an organic carboxylic acid salt, especially a citrate or lactate, amino acid(s), a mono- or disaccharide and/or a sugar alcohol. Further, it can also contain factor XIII derived from the starting material as well as optionally other plasma proteins, e.g. fibronectin or von Willebrand factor. The stabilized, deep-frozen **fibrinogen**-containing preparation contains less than 100 mmol/l, especially less than 50 mmol/l, of water-soluble inorganic salts.

ABEX UPTX: 20000712

SPECIFIC MATERIALS - 37 Stabilizing mixtures are specifically disclosed, e.g., 6 mg/ml Na3 citrate dihydrate, 0.12 mol/l L-arginine, pH 7.4.

L55 ANSWER 5 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 1999-407453 [35] WPIX

DNN N1999-303959 DNC C1999-120603

TI Peptide containing epitope recognized by anti-filaggrin antibodies, used as immunoassay reagents for diagnosis of rheumatoid polyarthritis.

DC B04 S03

IN ARNAUD, M; DALBON, P; GIRBAL, N E; JOLIVET, M; JOLIVET, R C; **SEBBAG, M; SERRE, G B R**; SIMON, M; VINCENT, C; GIRBAL-NEUHAUSER, E; JOLIVET-REYNAUD, C; **SERRE, G**

PA (INMR) BIO MERIEUX; (INMR) BIOMERIEUX SA

CYC 77

PI FR 2773157 A1 19990702 (199935)* 21p C07K014-47

WO 9935167 A1 19990715 (199935) FR C07K014-47

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW

W: AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP
KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US
UZ VN YU ZW

AU 9919717 A 19990726 (199952) C07K014-47

EP 1042366 A1 20001011 (200052) FR C07K014-47

R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

ADT FR 2773157 A1 FR 1997-16673 19971230; WO 9935167 A1 WO 1998-FR2899

19981229; AU 9919717 A AU 1999-19717 19981229; EP 1042366 A1 EP
 1998-964536 19981229, WO 1998-FR2899 19981229
 FDT AU 9919717 A Based on WO 9935167; EP 1042366 A1 Based on WO 9935167
 PRAI FR 1997-16673 19971230

IC ICM C07K014-47
 ICS A61K038-17; G01N033-53; G01N033-564
 AB FR 2773157 A UPAB: 19990902

NOVELTY - Peptide (I) contains an epitope, recognized by anti-filaggrin antibodies (Ab) present in the serum of patients with rheumatoid polyarthritis (RP), comprises a tripeptide motif centered on a **citrulline** (Cit) residue present in at least one of three peptides of 49, 14 and 14 amino acids (sequences reproduced; fragments of filaggrin).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) artificial antigen (AAg), recognized specifically by Ab, containing, or consisting of, at least one (I);
- (2) antigenic composition for diagnosis of RP containing at least one (I) or AAg, optionally labeled or conjugated to a carrier molecule; and
- (3) kits for detecting Ab containing (I) or AAg, plus suitable buffers and reagents.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - (I) are used as antigen for in vitro detection of Ab, for diagnosis of RP, in standard immunoassays.

ADVANTAGE - Ab are markers of RP and their detection makes possible diagnosis at an early stage.

Dwg.0/0

FS CPI EPI
 FA AB; DCN
 MC CPI: B11-C07A; B12-K04A
 EPI: S03-E14H4

TECH UPTX: 19990902

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred materials: (I) contain the motif Ser-Cit-His, particularly derived from the structure (Asp)n-X1-Ser-Arg-His-X2-(X3)n

n = 0 or 1;

X1 = Ser or Gly;

X2 = Ser or Pro;

X3 = Gly or Arg

. In (I), all amino acids are independently L or D forms, and one or more CONH bonds may be replaced by NHCO.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: (I) are produced:

- (1) by the action of peptidylarginine deiminase on Arg-containing substrates, which may be natural, recombinant or synthetic, or
- (2) directly by usual methods of peptide synthesis.

ABEX UPTX: 19990902

EXAMPLE - The peptide (A) of formula STGHSGSQHSHTTTQGRSDASRGSSGSRSTSRETRDQ EQSGDGSRRHSGS (amino acids 71-119 of human filaggrin) was synthesized conventionally then incubated for 30 min at 50degreesC with peptidylarginine deiminase (4 milliunits/mumole Arg) to convert Arg residues to **citrulline**. (A) was tested, before and after enzymatic treatment, for reactivity with a 1/2000 dilution of serum from a patient with rheumatoid polyarthritis by the dot-blot method (test antigen immobilized on nitrocellulose). (A) that had been treated was recognised by the serum.

L55 ANSWER 6 OF 8 WPIX (C) 2003 THOMSON DERWENT
 AN 1999-407426 [35] WPIX
 DNC C1999-120600
 TI Filaggrin-derived **citrulline** peptide antigens, useful for treatment of rheumatoid arthritis.

DC B04
 IN ARNAUD, M; DALBON, P; GIRBAL, N E; JOLIVET, M; JOLIVET, R C; **SEBBAG, M; SERRE, G B R**; SIMON, M; VINCENT, C; GIRBAL-NEUHAUSER, E; JOLIVET-REYNAUD, C; **SERRE, G**
 PA (UYTO-N) UNIV TOULOUSE SABATIER PAUL
 CYC 77
 PI FR 2773078 A1 19990702 (199935)* 26p A61K038-17
 WO 9934819 A2 19990715 (199935) EN 26p A61K038-17
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SZ UG ZW
 W: AL AU BA BB BG BR CA CN CU CZ EE GD GE HR HU ID IL IN IS JP KG KP
 KR LC LK LR LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR TT UA US
 UZ VN YU ZW
 AU 9919718 A 19990726 (199952) A61K038-17
 EP 1041997 A2 20001011 (200052) FR A61K038-17
 R: AT BE CH DE DK ES FI FR GB IE IT LI NL SE
 JP 2002500195 W 20020108 (200206) 27p A61K038-00
 EP 1041997 B1 20030416 (200328) FR A61K038-17
 R: AT BE CH DE DK ES FI FR GB IE IT LI NL SE
 ADT FR 2773078 A1 FR 1997-16672 19971230; WO 9934819 A2 WO 1998-FR2900
 19981229; AU 9919718 A AU 1999-19718 19981229; EP 1041997 A2 EP
 1998-964537 19981229, WO 1998-FR2900 19981229; JP 2002500195 W WO
 1998-FR2900 19981229, JP 2000-527267 19981229; EP 1041997 B1 EP
 1998-964537 19981229, WO 1998-FR2900 19981229
 FDT AU 9919718 A Based on WO 9934819; EP 1041997 A2 Based on WO 9934819; JP
 2002500195 W Based on WO 9934819; EP 1041997 B1 Based on WO 9934819
 PRAI FR 1997-16672 19971230
 IC ICM A61K038-00; A61K038-17
 ICS A61P037-00; C12N015-09
 ICA C07K014-47; C07K016-18
 ICI C07K014:47
 AB FR 2773078 A UPAB: 19990902
 NOVELTY - Filaggrin-derived **citrulline** peptide antigens are new.
 DETAILED DESCRIPTION - An antigenic peptide, specifically recognized
 by anti-filaggrin autoantibodies present in the serum of patients
 suffering from rheumatoid arthritis, constitutes a peptide derived from
 all or part of the sequence of a filaggrin unit. At least one arginine
 residue is substituted for **citrulline**. The peptide is used to
 obtain medicines to inhibit the autoantibodies from binding their
 antigenic target.
 An INDEPENDENT CLAIM is also included for a pharmaceutical
 composition for the treatment of rheumatoid arthritis characterized in
 that it contains as main agent at least one antigenic peptide as above.
 ACTIVITY - Anti-arthritic.
 MECHANISM OF ACTION - Anti-Filiggrin AutoAntibody Inhibitor.
 USE - The antigenic peptide is used to obtain medicines to inhibit
 anti-filiggrin autoantibodies from binding their antigenic target.
 Pharmaceutical compositions containing the **citrulline** peptides
 are used for the treatment of rheumatoid arthritis. All claimed.
 ADVANTAGE - For in vivo administration and use of the antigenic
 peptides, the amino acids can be changed to the L-forms (especially to
 increase protease resistance) as well as undergo other modifications to
 enhance their life in cells.
 Dwg.0/3
 FS CPI
 FA AB; DCN
 MC CPI: B04-N02; B11-C07A; B12-K04A
 TECH UPTX: 19990902
 TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Peptide: The antigenic
 peptide comprises all or part of a sequence derived from amino acids
 144-324, 76-144 or 71-119 of a human filaggrin unit, where at least one
 arginine residue is substituted for a **citrulline** residue. In
 particular the antigen comprises all or part of at least one sequence

chosen from the following (at least one arginine is substituted by a **citrulline**): STGHSGSQHS HTTTQGRSDA SRGSSGSRST SRETRDQEQS GDGSRHSGS; EQSADSSRHS GSGH; or ESSRDGSRHP RSHD. The antigenic peptides contain the tripeptide motif Ser-Cit-His, where Cit represents **citrulline**.

L55 ANSWER 7 OF 8 WPIX (C) 2003 THOMSON DERWENT
 AN 1998-207042 [18] WPIX
 DNN N1998-164439 DNC C1998-065259
 TI Artificial antigen recognised by anti-filaggrin auto-antibodies - is modified form of filaggrin with **citrulline** replacing at least one arginine, used for diagnosis of rheumatoid polyarthritis.
 DC B04 D16 S03
 IN ARNAUD, M; DALBON, P; GIRBAL NEUHAUSER, E; JOLIVET, M; JOLIVET, R C; **SEBBAG, M; SERRE, G**; SIMON, M; VINCENT, C; GIRBAL-NEUHAUSER, E; JOLIVET-REYNAUD, C
 PA (INMR) BIOMERIEUX SA
 CYC 20
 PI WO 9808946 A1 19980305 (199818)* FR 36p C12N015-12
 RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: CA US
 FR 2752842 A1 19980306 (199818) C07K014-78
 EP 929669 A1 19990721 (199933) FR C12N015-12
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
 ADT WO 9808946 A1 WO 1997-FR1541 19970901; FR 2752842 A1 FR 1996-10651 19960830; EP 929669 A1 EP 1997-938965 19970901, WO 1997-FR1541 19970901
 FDT EP 929669 A1 Based on WO 9808946
 PRAI FR 1996-10651 19960830
 IC ICM C07K014-78; C12N015-12
 ICS C07K014-47; C12N001-21; C12N009-78; G01N033-53; G01N033-532; G01N033-564; G01N033-68
 AB WO 9808946 A UPAB: 19980507
 Artificial antigen (Ag) recognised specifically by anti-filaggrin autoantibodies (Ab) present in the serum of patients with rheumatoid polyarthritis (RPA) is a recombinant or synthetic polypeptide containing at least part of a sequence derived from a filaggrin unit, or related molecule, by substitution of at least 1 arginine residue by **citrulline** (Cit).
 USE - Ag are used for in vitro diagnosis of RPA from complex formation with Ab in usual immunoassays.
 ADVANTAGE - Replacement of Arg by Cit is essential for antigen-specific recognition by Ab.
 Dwg.0/5
 FS CPI EPI
 FA AB
 MC CPI: B04-B04C2; B04-N02; B12-K04A; D05-H09; D05-H12B2; D05-H17A5
 EPI: S03-E14H4

L55 ANSWER 8 OF 8 WPIX (C) 2003 THOMSON DERWENT
 AN 1983-735953 [33] WPIX
 DNN N1983-142143 DNC C1983-077014
 TI Solid **fibrinogen** compsns. for use as tissue adhesive - contg. substance contg. urea or guanidine residue e.g. arginine.
 DC B04 P34
 IN BURK, W; FUHGE, P; HEIMBURGER, N; STOHR, H A
 PA (BEHW) BEHRINGWERKE AG
 CYC 22
 PI DE 3203775 A 19830811 (198333)* 10p
 EP 85923 A 19830817 (198334) DE
 R: AT BE CH DE FR GB IT LI LU NL SE
 JP 58135817 A 19830812 (198338)
 AU 8311105 A 19830811 (198339)
 NO 8300371 A 19830829 (198341)

FI 8300361 A 19830930 (198345)
 DK 8300444 A 19831010 (198347)
 ZA 8300726 A 19830913 (198403)
 PT 76193 A 19840507 (198422)
 ES 8403321 A 19840616 (198431)
 CA 1186995 A 19850514 (198524)
 IL 67823 A 19860131 (198610)
 DE 3366841 G 19861120 (198648)
 US 4650678 A 19870317 (198713)
 EP 85923 B 19861015 (199104) DE
 R: AT BE CH DE FR GB IT LI LU NL SE
 EP 85923 B2 19910123 (199104)
 R: BE CH DE FR GB IT LI LU NL SE
 JP 04007328 B 19920210 (199210)

ADT EP 85923 A EP 1983-100869 19830131; ZA 8300726 A ZA 1983-726 19830203; US 4650678 A US 1984-639617 19840810; JP 04007328 B JP 1983-15556 19830203

PRAI DE 1982-3203775 19820204

REP DE 3001435; DE 3002933; DE 3002934; 7.Jnl.Ref; DE 2461969; EP 35616

IC A61K015-06; A61K031-15; A61K035-16; A61K037-04; A61K047-16; A61L015-06; A61L017-00; C07G007-00; C12N009-48

AB DE 3203775 A UPAB: 19970820

Solid **fibrinogen** compsns. (I) contain in addn. to **fibrinogen** a substance contg. urea or guanidine residue. The preferred additive is arginine, which is pref. used in a concn. of 0.05-5 wt.%. The preparation advantageously additionally contain 0.1-5 wt.% of an amino acid with a hydrophobic side-chain or a water-soluble fatty acid. The preparation is pref packaged in a container under a gas atmosphere contg. at least 20 vol.% CO₂.

(I) are useful as adhesives for human tissues in the treatment of injuries to parenchymatous organs, bones or vessels. (I) need neither plasminogen activator inhibitor nor albumin as stabiliser, and are suitable for the preparation of highly concentrated (ca. 8%) solns. even at room temp. The additive urea or guanidine deriv. increases the solubility of **fibrinogen** lyophilisates and reduces the viscosity of the solns.

Dwg.0/0

FS CPI GMPI

FA AB

MC CPI: B04-B04D; B10-A13D; B10-A17; B12-A07

ABEQ EP 85923 B UPAB: 19930925

A solid **fibrinogen** formulation which contains, in addn. to **fibrinogen**, a substance contg. the urea or guanidine radical.

ABEQ US 4650678 A UPAB: 19930925

New readily dissolvable lyophilised **fibrinogen** compsn. comprises **fibrinogen** and 0.05-5 % wt. arginine, creatine, creatinine, glycochamine, urea or **citrulline**, pref. arginine. This dissolves easily to 2-14 % wt. aq. soln. Opt. also present is 0.1-5 % wt. amino acid with hydrophobic side chain (L-Lys) or water-sol. fatty acid (butyric) to increase soln. and opt. factor XIII (40-60U) and apoprotein, to increase resistance to tearing and inhibit **fibrinolysis**, respectively.

Compsn. may be prepd. by maintaining **fibrinogen** soln. at pH 5-8, temp. 0-15 deg.C, until **fibrinogen** polymers have pptd. out, sepn., and addn. of urea or guanidine radical, then drying.

USE/ADVANTAGE - As adhesive for human and animal tissues e.g. in treatment of injuries to parenchymal organs bones and vessels and as intravenous **fibrinogen** soln. for acute supply of **fibrinogen** for various diseases. Handling and storage advantages over cryoppts. and without need for inhibitor of plasminogen activator or albumin stabiliser giving longer of solns. at R.T.

=> fil medline

FILE 'MEDLINE' ENTERED AT 10:40:44 ON 29 JUN 2003

FILE LAST UPDATED: 28 JUN 2003 (20030628/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L70 ANSWER 1 OF 2 MEDLINE
AN 2003131708 MEDLINE
DN 22532801 PubMed ID: 12645351
TI [Early diagnosis of **rheumatoid arthritis** with a test based upon a specific antigen: cyclic **citrullinated** peptide].
Vroegdiagnostiek van reumatoïde artritis met een test op basis van een specifiek antigeen: cyclisch **gecitrullineerd** peptide.
CM Comment in: Ned Tijdschr Geneesk. 2003 Apr 12;147(15):729-30; author reply 730-1
AU van Venrooij W J; van de Putte L B A
CS Katholieke Universiteit, faculteit Natuurwetenschappen, Wiskunde en Informatica, afd. Biochemie, Postbus 9101, 6500 HB Nijmegen..
w.vanvenrooij@ncmls.kun.nl
SO NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (2003 Feb 1) 147 (5) 191-4. Ref: 22
Journal code: 0400770. ISSN: 0028-2162.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Dutch
FS Priority Journals
EM 200305
ED Entered STN: 20030321
Last Updated on STN: 20030515
Entered Medline: 20030514
AB In patients with **rheumatoid arthritis** (RA), joint erosions occur at a very early stage of the disease before clinical symptoms can be detected. Early treatment with currently available **antirheumatic** drugs may stop or delay the development of such erosions. A simple and specific diagnostic test is needed for treatment to be initiated at an early stage. The specificity of the routinely used **rheumatoid** factor (RF) test is too low for that purpose. A novel autoantibody, directed to **citrullinated** antigens in the synovium, seems to provide a new starting point. These **citrullinated** autoantigens (e.g. **fibrin**) are specifically present in inflamed synovia and the antibodies for these are locally produced. The autoantibodies can be detected in the blood of the patients with RA years before the first clinical signs are manifest, and high titres appear to correlate strongly with erosive disease. The test for cyclic **citrullinated** peptide, which has recently become available, has a specificity of 98-99% and a sensitivity of 75-80%.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Arthritis, Rheumatoid: DI, diagnosis
*Arthritis, Rheumatoid: IM, immunology
*Autoantibodies: BL, blood
Autoantibodies: IM, immunology
Autoantigens: DU, diagnostic use

*Autoantigens: IM, immunology
 *Citrulline: IM, immunology
 Diagnosis, Differential
 English Abstract
 Peptides, Cyclic: IM, immunology
 Rheumatoid Factor: DU, diagnostic use
 Sensitivity and Specificity
 Synovial Membrane: IM, immunology
 Synovial Membrane: PA, pathology

RN 372-75-8 (Citrulline); 9009-79-4 (Rheumatoid Factor)
 CN 0 (Autoantibodies); 0 (Autoantigens); 0 (Peptides, Cyclic)

L70 ANSWER 2 OF 2 MEDLINE

AN 2001259480 MEDLINE

DN 21136399 PubMed ID: 11238669

TI The major synovial targets of the **rheumatoid arthritis**
 -specific antifilaggrin autoantibodies are deiminated forms of the alpha-
 and beta-chains of **fibrin**.

AU Masson-Bessiere C; Sebbag M; Girbal-Neuhauser E; Nogueira L; Vincent C;
 Senshu T; Serre G

CS Department of Biology and Pathology of the Cell, Institut National de la
 Sante et de la Recherche Medicale Contrat Jeune Formation 96-02,
 Toulouse-Purpan School of Medicine, University Toulouse III, Toulouse,
 France.

SO JOURNAL OF IMMUNOLOGY, (2001 Mar 15) 166 (6) 4177-84.
 Journal code: 2985117R. ISSN: 0022-1767.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200105

ED Entered STN: 20010521

Last Updated on STN: 20010521

Entered Medline: 20010517

AB IgG antifilaggrin autoantibodies (AFA) are the most specific serological
 markers of **rheumatoid arthritis**. In epithelial
 tissues, they recognize **citrulline**-bearing epitopes present on
 various molecular forms of (pro)filaggrin. Histological analysis of
rheumatoid synovial membranes with an Ab to **citrulline**
 showed labeling of interstitial amorphous deposits and mononuclear cells
 of various types. Immunochemical analysis of exhaustive sequential
 extracts of the same tissues showed that they contain several deiminated (
citrulline containing) proteins. Among them, two proteins,
 p64--78 and p55--61, present in urea-DTT and guanidine extracts, were
 shown by immunoblotting to be specifically targeted by AFA. By
 amino-terminal sequencing the proteins were identified as deiminated forms
 of the alpha- and beta-chains of **fibrin**, respectively. Their
 identity was confirmed using several Abs specific for the A alpha- and/or
 to the B beta-chain of **fibrin**(ogen). Moreover, AFA-positive
rheumatoid arthritis (RA) sera and purified AFA were
 highly reactive to the A alpha- and B beta-chains of human
fibrinogen only after deimination of the molecules by a
 peptidylarginine deiminase. Autoantibodies affinity purified from a pool
 of RA sera onto deiminated **fibrinogen** were reactive toward all
 of the epithelial and synovial targets of AFA. This confirmed that the
 autoantibodies to the deiminated A alpha- and B beta-chains of
fibrinogen, the autoantibodies to the synovial proteins p64--78
 and p55--61, and, lastly, AFA, constitute largely overlapping autoantibody
 populations. These results show that deiminated forms of **fibrin**
 deposited in the **rheumatoid** synovial membranes are the major
 target of AFA. They suggest that autoimmunization against deiminated
fibrin is a critical step in RA pathogenesis.

CT Check Tags: Animal; Human; Support, Non-U.S. Gov't

Antigen-Antibody Reactions

*Arthritis, Rheumatoid: IM, immunology

Arthritis, Rheumatoid: PA, pathology

*Autoantibodies: ME, metabolism

Autoantigens: CH, chemistry

*Autoantigens: IM, immunology

Autoantigens: ME, metabolism

Epitopes: IM, immunology

Epitopes: ME, metabolism

Fibrin: CH, chemistry

Fibrin: IM, immunology

*Fibrin: ME, metabolism

Fibrinogen: CH, chemistry

Fibrinogen: IM, immunology

Fibrinogen: ME, metabolism

*Imines: ME, metabolism

Immunohistochemistry

Intermediate Filament Proteins: CH, chemistry

*Intermediate Filament Proteins: IM, immunology

Intermediate Filament Proteins: ME, metabolism

Peptide Fragments: CH, chemistry

Peptide Fragments: IM, immunology

Peptide Fragments: ME, metabolism

Rats

Synovial Membrane: CH, chemistry

*Synovial Membrane: IM, immunology

Synovial Membrane: ME, metabolism

RN 9001-31-4 (Fibrin); 9001-32-5 (Fibrinogen)

CN 0 (Autoantibodies); 0 (Autoantigens); 0 (Epitopes); 0 (Imines); 0 (Intermediate Filament Proteins); 0 (Peptide Fragments); 0 (filaggrin)

=> fil biosis

FILE 'BIOSIS' ENTERED AT 10:47:42 ON 29 JUN 2003

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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 25 June 2003 (20030625/ED)

=> d all tot 191

L91 ANSWER 1 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2001:390353 BIOSIS

DN PREV200100390353

TI The diagnostic properties of **rheumatoid arthritis**
antibodies recognizing a cyclic **citrullinated** peptide.AU Schellekens, Gerard A.; Visser, Hendrik; de Jong, Ben A. W.; van den
Hoogen, Frank H. J.; Hazes, Johanna M. W.; Breedveld, Ferdinand C.; van
Venrooij, Walther J. (1)CS (1) Department of Biochemistry, University of Nijmegen, 161, 6500 HB,
Nijmegen NetherlandsSO Arthritis & Rheumatism, (January, 2000) Vol. 43, No. 1, pp.
155-163. print.

ISSN: 0004-3591.

DT Article

LA English

SL English

AB Objective. Since modern treatment of **rheumatoid**
arthritis (RA) is shifting toward aggressive **antirheumatic**

therapy in an early phase of the disease, diagnostic tests with high specificity are desirable. A new serologic test (anti-cyclic **citrullinated** peptide (anti-CCP) enzyme-linked immunosorbent assay (ELISA)) was developed to determine the presence of **antibodies** directed toward **citrullinated** peptides, using a synthetic peptide designed for this purpose. Methods. A cyclic peptide variant that contains deiminated **arginine** (**citrulline**) was designed and used as antigenic substrate in ELISA. Test parameters and diagnostic characteristics of the test were studied in patients with and without RA, in patients with various infectious diseases, and in a group of patients from an early **arthritis** clinic (EAC). Results. Using prevalent RA and non-RA sera, the anti-CCP ELISA proved to be extremely specific (98%), with a reasonable sensitivity (68%). Also, in the EAC study group, the anti-CCP ELISA appeared to be highly specific for RA (96%). In comparison with the IgM **rheumatoid** factor (IgM-RF) ELISA, the anti-CCP ELISA had a significantly higher specificity (96% for CCP versus 91% for IgM-RF; $P = 0.016$) at optimal cut-off values. The sensitivity of both tests for RA was moderate: 48% and 54% for the anti-CCP ELISA and the IgM-RF ELISA, respectively ($P = 0.36$). Combination of the anti-CCP and the IgM-RF ELISAs resulted in a significantly higher positive predictive value of 91% ($P = 0.013$) and a slightly lower negative predictive value of 78% ($P = 0.35$) as compared with the use of the IgM-RF ELISA alone. The ability of the 2 tests performed at the first visit to predict erosive disease at 2 years of followup in RA patients was comparable (positive predictive value 91%). Conclusion. The anti-CCP ELISA might be very useful for diagnostic and therapeutic strategies in RA of recent onset.

CC Pathology, General and Miscellaneous - Diagnostic *12504

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006

Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508

Allergy *35500

BC Hominidae 86215

IT Major Concepts

Rheumatology (Human Medicine, Medical Sciences); Methods and Techniques

IT Diseases

inflammatory arthropathy: differential diagnosis, joint disease;

rheumatoid arthritis: connective tissue disease,

differential diagnosis, immune system disease, joint disease

IT Chemicals & Biochemicals

IgM **rheumatoid** factor [immunoglobulin M **rheumatoid** factor]

IT Alternate Indexing

Arthritis, Rheumatoid (MeSH)

IT Methods & Equipment

anti-cyclic **citrullinated** peptide ELISA: diagnostic method, sensitivity, specificity

IT Miscellaneous Descriptors

early **arthritis** clinic

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae): patient

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 2 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2001:390352 BIOSIS

DN PREV200100390352

TI **Anticitrulline antibody** assay specificity for **rheumatoid arthritis**: Comment on the article by Schellekens et al.

AU Berthelot, Jean-Marie (1); Saraux, Alain
 CS (1) Nantes University Hospital, Nantes France
 SO Arthritis & Rheumatism, (August, 2000) Vol. 43, No. 8, pp.
 1901-1902. print.
 ISSN: 0004-3591.
 DT Letter
 LA English
 SL English
 CC Clinical Biochemistry; General Methods and Applications *10006
 Pathology, General and Miscellaneous - Diagnostic *12504
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
***34508**
 Allergy *35500
 BC Hominidae 86215
 IT Major Concepts
 Clinical Chemistry (Allied Medical Sciences); **Rheumatology**
 (Human Medicine, Medical Sciences); Methods and Techniques
 IT Diseases
rheumatoid arthritis: connective tissue disease,
 diagnosis, immune system disease, joint disease
 IT Chemicals & Biochemicals
anticitrulline antibodies; antiperinuclear factor;
rheumatoid factor
 IT Alternate Indexing
Arthritis, Rheumatoid (MeSH)
 IT Methods & Equipment
 ELISA: analytical method; **anticitrulline antibody**
 assay: diagnostic method, specificity
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 3 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2001:389518 BIOSIS
 DN PREV200100389518
 TI The prognostic value of anti-cyclic **citrullinated** peptide
antibody in patients with recent-onset **rheumatoid**
arthritis.
 AU Kroot, Eric-Jan J. A.; de Jong, Ben A. W.; van Leeuwen, Miek A.; Swinkels,
 Hilde; van den Hoogen, Frank H. J.; van 't Hof, Martin; van de Putte, Leo
 B. A.; van Rijswijk, Martin H.; van Venrooij, Walther J.; van Riel, Piet
 L. C. M. (1)
 CS (1) Department of Rheumatology, University Hospital Nijmegen, 6500 HB,
 Nijmegen Netherlands
 SO Arthritis & Rheumatism, (August, 2000) Vol. 43, No. 8, pp.
 1831-1835. print.
 ISSN: 0004-3591.
 DT Article
 LA English
 SL English
 AB Objective: To study the predictive value of anti-cyclic
citrullinated peptide **antibody** (anti-CCP) in patients
 with recent-onset **rheumatoid arthritis** (RA). Methods:
 Outcome in terms of physical disability (Health Assessment Questionnaire)
 and radiologic damage (modified Sharp method) over 3-year and 6-year
 periods was determined in an inception cohort of 273 RA patients who had
 had disease symptoms for <1 year at study entry. Anti-CCP titers were
 determined at baseline and considered positive as recently described.

Their prognostic value was studied by means of multiple regression analysis, in which anti-CCP positivity, sex, age at study entry, IgM **rheumatoid** factor (IgM-RF) status, Disease Activity Score (DAS), HLA-DR4 status, and (in a separate group of patients) shared epitope status were used as independent variables, and radiologic damage and functional disability as dependent variables. Results: Patients with anti-CCP had developed significantly more severe radiologic damage after 6 years of followup. In multiple regression analysis, radiologic damage after 6 years followup was significantly predicted by IgM-RF status, radiologic score at entry, and anti-CCP status. Functional disability was significantly predicted by sex, age at entry, IgM-RF status, and DAS. Conclusion: Our data show that in almost 70% of RA patients, anti-CCP **antibody** is present at the early stages of disease.

Anti-CCP-positive patients developed significantly more severe radiologic damage than patients who were anti-CCP negative, although in multiple regression analysis the additional predictive value was rather moderate.

CC Clinical Biochemistry; General Methods and Applications *10006

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006

Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508

Allergy *35500

BC Hominidae 86215

IT Major Concepts

Clinical Chemistry (Allied Medical Sciences); **Rheumatology**
(Human Medicine, Medical Sciences)

IT Diseases

rheumatoid arthritis: connective tissue disease,
immune system disease, joint disease, prognosis, recent-onset

IT Chemicals & Biochemicals

IgM **rheumatoid** factor [immunoglobulin M **rheumatoid**
factor]; anti-cyclic **citrullinated** peptide **antibody**
: prognostic value

IT Alternate Indexing

Arthritis, Rheumatoid (MeSH)

IT Methods & Equipment

radiography: imaging method

IT Miscellaneous Descriptors

Disease Activity Score; HLA-DR4 status; physical disability

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae): patient

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 4 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 2001:383150 BIOSIS

DN PREV200100383150

TI (Untitled.

AU Hazes, Johanna M. M. (1); van Venrooij, Walther J.

CS (1) University Hospital Leiden, Leiden Netherlands

SO Arthritis & Rheumatism, (August, 2000) Vol. 43, No. 8, pp. 1902.
print.

ISSN: 0004-3591.

DT Letter

LA English

SL English

CC Clinical Biochemistry; General Methods and Applications *10006

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006

Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508

Allergy *35500
 BC Hominidae 86215
 IT Major Concepts
 Clinical Chemistry (Allied Medical Sciences); **Rheumatology**
 (Human Medicine, Medical Sciences); Methods and Techniques
 IT Diseases
 rheumatoid arthritis: connective tissue disease,
 diagnosis, immune system disease, joint disease
 IT Chemicals & Biochemicals
 anti-cyclic **citrullinated** peptide; **anticitrulline**
 antibodies; antiperinuclear factor; **rheumatoid** factor
 IT Alternate Indexing
 Arthritis, Rheumatoid (MeSH)
 IT Methods & Equipment
 ELISA: analytical method, negative predictive value, positive
 predictive value, specificity
 IT Miscellaneous Descriptors
 single test diagnosis
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 5 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2001:92726 BIOSIS
 DN PREV200100092726
 TI Increased nitric oxide production in patients with systemic sclerosis.
 AU Sud, Archana (1); Khullar, Madhu; Wanchu, Ajay; Bamberg, Pradeep
 CS (1) Department of Internal Medicine (Rheumatology Unit), Post Graduate
 Institute of Medical Education and Research (PGIMER), Chandigarh, 160012:
 asud@doctor.com India
 SO Nitric Oxide, (2000) Vol. 4, No. 6, pp. 615-619. print.
 ISSN: 1089-8603.
 DT Article
 LA English
 SL English
 AB Nitric oxide (NO, nitrogen monoxide) is a messenger molecule whose
 synthesis can be induced by proinflammatory cytokines. Increased
 production of NO has been reported in various inflammatory and autoimmune
 diseases. We studied serum nitrite and **citrulline** as surrogate
 markers for NO production in patients with systemic sclerosis (SSc) and
 looked for correlation with extent of disease, disease duration, age, and
 systemic involvement. Thirty-four patients were studied against 20
 controls. The nitrite levels were significantly higher in the disease
 group (1588.4 \pm 998.2 nmol/ml compared to 327.8 \pm 137.7 nmol/ml; $P <$
 0.001). The **citrulline** levels of the disease group were also
 significantly higher (5490.1 \pm 2518.3 nmol/ml compared to 3264.5 \pm
 2509.7 nmol/ml in the controls; $P = 0.005$). There was no significant
 difference among limited and diffuse subgroups. There was no significant
 difference in patients with or without **arthritis** or interstitial
 lung disease or with other systemic involvement. On multivariate analysis
 there was a trend toward a rising level of nitrite with worsening lung
 functions ($P = 0.07$). Hence, there is evidence of increased NO production
 in patients with SSc. There is no difference between NO levels in disease
 subgroups or those with systemic involvement.

CC Biochemical Studies - General *10060
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
 *18006
 BC Hominidae 86215
 IT Major Concepts
 Biochemistry and Molecular Biophysics; **Rheumatology** (Human

Medicine, Medical Sciences)

IT Diseases
progressive systemic sclerosis: connective tissue disease

IT Chemicals & Biochemicals
nitric oxide: increased production

IT Alternate Indexing
Scleroderma, Systemic (MeSH)

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): patient

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 10102-43-9 (NITRIC OXIDE)

L91 ANSWER 6 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:31776 BIOSIS
DN PREV200100031776
TI Progress in the use of biochemical and biological markers for evaluation
of **rheumatoid arthritis**.
AU Nakamura, Robert M. (1)
CS (1) Department of Pathology, Scripps Clinic, La Jolla, CA, 92037 USA
SO Journal of Clinical Laboratory Analysis, (2000) Vol. 14, No. 6, pp.
305-313. print.
ISSN: 0887-8013.
DT General Review
LA English
SL English
AB **Rheumatoid arthritis** (RA) is a chronic systemic
inflammatory autoimmune disorder which is predominant in females. The
exact etiology remains undefined. Recently, a large number of biochemical
and biologic markers, which are useful in the diagnosis, prognosis, and
monitoring therapy of RA, have been reported. The new markers include
genetic markers, **filaggrin**, **citrulline** containing
peptides, A2/RA 33, cytokines, joint and collagen breakdown products, and
bone turnover markers. No laboratory tests in and of themselves are
diagnostic of RA. The new markers have been employed in monitoring RA
patients during treatment and following the course of the disease. With
the development of innovative therapies for RA, many of the biochemical
and biologic markers will be useful.

CC **Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology**
***18006**
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
***34508**
Allergy *35500

BC Hominidae 86215

IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences);
Rheumatology (Human Medicine, Medical Sciences)

IT Diseases
erosive joint disease: joint disease; **rheumatoid**
arthritis: connective tissue disease, diagnosis, evaluation,
immune system disease, joint disease, prognosis

IT Chemicals & Biochemicals
A2/RA 33: biological marker; bone turnover marker: biological marker;
citrulline containing peptides: biological marker; collagen:
biological marker; cytokines: biological marker; **filaggrin**:
biological marker; genetic markers: biological marker

IT Alternate Indexing
Arthritis, Rheumatoid (MeSH)

IT Methods & Equipment

monitoring therapy: therapeutic method
IT Miscellaneous Descriptors
inflammation
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 7 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:513470 BIOSIS
DN PREV200000513470
TI Elevated nitric oxide production in patients with primary Sjogren's syndrome.
AU Wanchu, A. (1); Khullar, M.; Sud, A.; Bambery, P.
CS (1) Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, 160012 India
SO Clinical Rheumatology, (2000) Vol. 19, No. 5, pp. 360-364. print.
ISSN: 0770-3198.
DT Article
LA English
SL English
AB Nitric oxide (NO) production is elevated in patients with inflammatory disorders. We have previously shown increased NO production in patients with **rheumatoid** arthritis and systemic lupus erythematosus. In this study we used nitrite and **citrulline** levels as surrogate markers of NO production in patients with primary Sjogren's syndrome (SS) and measured their levels by spectrophotometry. Fifteen patients and 15 age- and sex-matched controls were studied. Mean nitrite levels in patients were 582.3 +- 208.3 nmol/ml, but those in controls were significantly lower, at 203.2 +- 106.9 nmol/ml (p<0.001). **Citrulline** levels were 2820.4+-933.9 nmol/ml in patients and were significantly higher than 217.4+-144.8 nmol/ml, the levels in controls (p<0.0001). Mean levels of both nitrite and **citrulline** were significantly higher in patients with **arthritis** than in those who had no joint manifestations (p<0.05). There was no correlation between NO production and other variables, such as age, disease duration, drug therapy and antinuclear **antibodies** or **rheumatoid** factor positivity. Increased NO production may be partly a reflection of the presence of **arthritis** in five patients. It is concluded that there is increased NO production in patients with primary SS, especially if they have associated **arthritis**.
CC Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Clinical Biochemistry; General Methods and Applications *10006
Biochemical Studies - General *10060
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
Dental and Oral Biology - Pathology *19006
Sense Organs, Associated Structures and Functions - Pathology *20006
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Hominidae 86215
IT Major Concepts
Clinical Chemistry (Allied Medical Sciences); **Rheumatology**
(Human Medicine, Medical Sciences)
IT Diseases
primary Sjogren's syndrome: connective tissue disease, dental and oral disease, eye disease, immune system disease, joint disease
IT Chemicals & Biochemicals
citrulline; nitric oxide: elevated production; nitrite
IT Miscellaneous Descriptors
clinical profile

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 372-75-8 (**CITRULLINE**)
10102-43-9 (NITRIC OXIDE)
14797-65-0 (NITRITE)

L91 ANSWER 8 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:495010 BIOSIS
DN PREV200000495131
TI HLA class II polymorphism, **rheumatoid arthritis**
outcome and influence of the treatment.
AU Lard, L. (1); Vos, K. (1); Visser, H. (1); Hazes, M. (1); Breedveld, F.
(1); Schreuder, G.; de Vries, R.; Zanelli, E.
CS (1) Dept of Rheumatology, Leiden University Medical Center, Leiden
Netherlands
SO Human Immunology, (2000) Vol. 61, No. Supplement 2, pp. S9. print.
Meeting Info.: 26th Annual Meeting of the American Society for
Histocompatibility and Immunogenetics Lake Buena Vista, Florida, USA
October 10-14, 2000 American Society for Histocompatibility and
Immunogenetics
. ISSN: 0198-8859.
DT Conference
LA English
SL English
CC **Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology**
***18006**
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
Genetics and Cytogenetics - General *03502
Genetics and Cytogenetics - Human *03508
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
***34508**
Allergy *35500
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Molecular Genetics (Biochemistry
and Molecular Biophysics); Clinical Immunology (Human Medicine, Medical
Sciences)
IT Diseases
rheumatoid arthritis: connective tissue disease,
immune system disease, joint disease
IT Chemicals & Biochemicals
HLA: class II, polymorphism; HLA-DQB1; HLA-DRB1; cfc1:
citrulline-containing peptide; **rheumatoid** factor
IT Alternate Indexing
Arthritis, Rheumatoid (MeSH)
IT Methods & Equipment
ELISA: measurement method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 9 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:167969 BIOSIS
DN PREV200000167969
TI Combination of HLA class II typing and an anti-citrulline
-containing peptide ELISA predicts outcome in early **rheumatoid**
arthritis.
AU Zanelli, E. (1); Vos, K. (1); Schellekens, G. (1); Visser, H. (1); Hazes,
M. (1); Breedveld, F. (1); Schreuder, G. (1); de Jong, B. (1); van
Venrooij, W. (1); de Vries, R. (1)
CS (1) Dept of Immunohaematology, Leiden University Medical Centre, Leiden
Netherlands
SO Human Immunology., (2000) Vol. 61, No. Suppl. 1, pp. S15.
Meeting Info.: 14th European Histocompatibility Conference. Montpellier,
France April 04-07, 2000
ISSN: 0198-8859.
DT Conference
LA English
SL English
CC **Immunology and Immunochemistry - General; Methods *34502**
Genetics and Cytogenetics - Human *03508
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
*18001
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Immune
System (Chemical Coordination and Homeostasis); Skeletal System
(Movement and Support)
IT Diseases
rheumatoid arthritis: connective tissue disease,
immune system disease, joint disease, remission, severity
IT Chemicals & Biochemicals
HLA class II: haplotype; **citrulline**-containing peptides:
antibody
IT Alternate Indexing
Arthritis, Rheumatoid (MeSH)
IT Methods & Equipment
ELISA: detection method, detection/labeling techniques
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 10 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:89027 BIOSIS
DN PREV200000089027
TI Nitric oxide production is increased in patients with inflammatory
myositis.
AU Wanchu, A. (1); Khullar, M.; Sud, A.; Bamberg, P.
CS (1) Department of Internal Medicine, Postgraduate Institute of Medical
Education and Research, Chandigarh, 160012 India
SO Nitric Oxide, (1999) Vol. 3, No. 6, pp. 454-458.
ISSN: 1089-8603.
DT Article
LA English
SL English

- AB Nitric oxide (NO) production is increased in several inflammatory disorders. We have previously demonstrated higher levels of NO production among patients with **rheumatoid arthritis** and systemic lupus erythematosus. In this study we measured serum levels of nitrite and **citrulline** using calorimetric methods as surrogate markers of NO production among patients with inflammatory myositis (IM). Twenty patients with IM and 19 age- and sex-matched controls were studied. Serum nitrite levels were significantly higher among patients than among controls (986.6 \pm 880 and 204.3 \pm 113.9 nmol/ml, respectively; $P = 0.001$). Serum **citrulline** levels, too, were significantly higher among patients than among controls (3755.7 \pm 1905.5 and 189 \pm 177.2 nmol/ml, respectively; $P < 0.0001$). There was a positive correlation between steroid dosage and serum **citrulline** levels ($r = 0.51$, $P = 0.036$) and a negative correlation between steroid dosage and disease duration ($r = -0.54$, $P = 0.025$). It was concluded that NO production is increased in patients with IM and those with more active disease, as indicated by higher steroid dosage, have higher serum **citrulline** levels.
- CC **Immunology and Immunochemistry - General; Methods *34502**
 Biochemical Studies - General *10060
 Muscle - General; Methods *17501
- BC Hominidae 86215
- IT Major Concepts
 Immune System (Chemical Coordination and Homeostasis); Muscular System (Movement and Support)
- IT Diseases
 inflammatory myositis: immune system disease, muscle disease;
rheumatoid arthritis: connective tissue disease, immune system disease, joint disease; systemic lupus erythematosus: connective tissue disease, immune system disease
- IT Chemicals & Biochemicals
citrulline; nitric oxide: production; nitrite
- IT Alternate Indexing
Arthritis, Rheumatoid (MeSH); Lupus Erythematosus, Systemic (MeSH)
- IT Methods & Equipment
 calorimetry: analytical method
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 human (Hominidae): patient
- ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
- RN 372-75-8 (**CITRULLINE**)
 10102-43-9 (NITRIC OXIDE)
 14797-65-0 (NITRITE)
- L91 ANSWER 11 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- AN 1999:535832 BIOSIS
- DN PREV199900535832
- TI Markers of nitric oxide production in **rheumatoid** synovial fluid.
- AU Holm, P. (1); Leirisalo-Repo, M. (1); Tuomiranta, T. (1); Kankaanranta, H. (1); Moilanen, E. (1)
- CS (1) Medical School, University of Tampere, Tampere Finland
- SO Acta Physiologica Scandinavica, (**Sept.**, 1999) Vol. 167, No. SUPPL. 645, pp. 49.
 Meeting Info.: Scientific Committees of the Sixth International Meeting on Biology of Nitric Oxide Stockholm, Sweden September 5-8, 1999 Scandinavian Physiological Society
 . ISSN: 0001-6772.
- DT Conference
- LA English
- CC Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001

Biochemical Studies - General *10060
 Metabolism - General Metabolism; Metabolic Pathways *13002
Immunology and Immunochemistry - General; Methods *34502
Blood, Blood-Forming Organs and Body Fluids - General; Methods
***15001**
 General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annuals *00520
 BC Hominidae 86215
 IT Major Concepts
 Clinical Chemistry (Allied Medical Sciences); **Rheumatology**
 (Human Medicine, Medical Sciences)
 IT Parts, Structures, & Systems of Organisms
 synovial fluid: skeletal system
 IT Diseases
 rheumatoid arthritis: connective tissue disease,
 immune system disease, joint disease
 IT Chemicals & Biochemicals
 arginine: serum; **citrulline:** serum; nitric oxide:
 production; nitrite: serum; peroxynitrite: production; C-reactive
 protein: serum
 IT Alternate Indexing
 Arthritis, Rheumatoid (MeSH)
 IT Miscellaneous Descriptors
 Meeting Abstract; Meeting Poster
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
 RN 74-79-3Q (**ARGININE**)
 7200-25-1Q (**ARGININE**)
 372-75-8 (**CITRULLINE**)
 10102-43-9 (NITRIC OXIDE)
 14797-65-0 (NITRITE)
 19059-14-4 (PEROXYNITRITE)

L91 ANSWER 12 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1999:535423 BIOSIS
 DN PREV199900535423
 TI The prognostic value of the antiperinuclear factor, determined by a
 recently developed peptide-based ELISA, using anti **citrulline**
 -containing peptide **antibodies** (anti-CCP) in patients with
 recent onset **Rheumatoid Arthritis**.
 AU Kroot, E. (1); Schellekens, G. (1); Swinkels, H. (1); van den Hoogen, F.
 (1); van 't Hof, M. (1); van e Putte, L. (1); van Venrooij, W. (1); van
 Riel, P. (1)
 CS (1) Nijmegen Netherlands
 SO Arthritis & Rheumatism, (**Sept., 1999**) Vol. 42, No. 9 SUPPL., pp.
 S179.
 Meeting Info.: 63rd Annual Scientific Meeting of the American College of
 Rheumatology and the 34th Annual Scientific Meeting of the Association of
 Rheumatology Health Professionals Boston, Massachusetts, USA November
 13-17, 1999
 ISSN: 0004-3591.
 DT Conference
 LA English
 CC **Immunology and Immunochemistry - Immunopathology, Tissue Immunology**
***34508**
 Metabolism - Carbohydrates *13004
 Metabolism - Proteins, Peptides and Amino Acids *13012
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**

General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Methods - Carbohydrates *10058
Immunology and Immunochemistry - General; Methods *34502
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Carbohydrates *10068
Enzymes - Methods *10804
Pathology, General and Miscellaneous - Inflammation and Inflammatory
Disease *12508
BC Hominidae 86215
IT Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences);
Rheumatology (Human Medicine, Medical Sciences)
IT Diseases
recent onset **rheumatoid arthritis**: connective
tissue disease, immune system disease, prognosis, joint disease
IT Chemicals & Biochemicals
antiperinuclear factor **autoantibody**: prognostic value
IT Methods & Equipment
peptide-based ELISA: anti-**citrulline**-containing
antibody use, immunological method
IT Miscellaneous Descriptors
Meeting Abstract
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 13 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:528415 BIOSIS
DN PREV199900528415
TI **Rheumatoid** sera potentially recognize all **citrullinated**
proteins.
AU Lapointe, Elvy (1); Dery, Ugo; Vaillancourt, Francois; Menard, Henri A.;
Senshu, Tatsuo
CS (1) Sherbrooke, PQ Canada
SO Arthritis & Rheumatism, (**Sept.**, 1999) Vol. 42, No. 9 SUPPL., pp.
S86.
Meeting Info.: 63rd Annual Scientific Meeting of the American College of
Rheumatology and the 34th Annual Scientific Meeting of the Association of
Rheumatology Health Professionals Boston, Massachusetts, USA November
13-17, 1999
ISSN: 0004-3591.
DT Conference
LA English
CC **Immunology and Immunochemistry - General; Methods *34502**
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
BC Leporidae 86040
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
rheumatoid sera: blood and lymphatics; skeletal muscle:
muscular system
IT Diseases
rheumatoid arthritis: connective tissue disease,
immune system disease, joint disease
IT Chemicals & Biochemicals

bovine serum albumin; **citrullinated** proteins; histone 1;
 myelin basic protein; peptidyl **arginine** deiminase

IT Alternate Indexing
Arthritis, Rheumatoid (MeSH)

IT Miscellaneous Descriptors
 Meeting Abstract; Meeting Poster

ORGN Super Taxa
 Leporidae: Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 rabbit (Leporidae)

ORGN Organism Superterms
 Animals; Chordates; Lagomorphs; Mammals; Nonhuman Mammals; Nonhuman
 Vertebrates; Vertebrates

RN 75536-80-0 (PEPTIDYL **ARGININE** DEIMINASE)

L91 ANSWER 14 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1999:468960 BIOSIS
 DN PREV199900468960
 TI Elevated urinary nitrite and **citrulline** levels in patients with
rheumatoid arthritis.

AU Wanchu, A. (1); Khullar, M.; Sud, A.; Deodhar, S. D.; Bambery, P.
 CS (1) Department of Internal Medicine, Postgraduate Institute of Medical
 Education and Research, Chandigarh, 160012 India
 SO Inflammopharmacology, (1999) Vol. 7, No. 2, pp. 155-161.
 ISSN: 0925-4692.

DT Article
 LA English
 SL English

AB The objective of this research was to determine if NO production, as
 measured in the serum and urine, is increased in patients with
rheumatoid arthritis. Forty-seven patients with RA were
 recruited in the study and subdivided into inactive and active disease (24
 and 23 patients, respectively). Twenty-eight healthy individuals served as
 controls and nine patients with gastroenteritis were studied to validate
 the technique of measurement of NO production. Nitrite and
citrulline were measured by spectrophotometry, as surrogate
 markers of NO production. It was found that serum nitrite and
citrulline levels of patients with gastroenteritis were not
 significantly different from controls and the two subgroups of RA. Urine
 nitrite and **citrulline** levels were significantly higher in
 patients with gastroenteritis as compared to the two subgroups of RA and
 controls ($p < 0.001$). Serum and urine nitrite levels of patients with
 active RA were higher than controls and patients with inactive disease ($p < 0.05$). Serum **citrulline** levels were not significantly different
 among the two subgroups of patients with RA. However, they were
 significantly higher in patients with active disease as compared with
 controls ($p < 0.05$). Urinary **citrulline** levels were
 significantly higher among patients with active disease as compared to
 controls and patients with inactive RA ($p < 0.05$). It is therefore
 suggested that urinary nitrite and **citrulline** levels can be
 useful for the measurement of NO production and are associated with active
 disease in patients with RA.

CC **Immunology and Immunochemistry - General; Methods *34502**
 Biochemical Studies - General *10060
 Biophysics - General Biophysical Studies *10502
 Digestive System - General; Methods *14001
 Urinary System and External Secretions - General; Methods *15501
 Endocrine System - General *17002

IT Major Concepts
 Biochemistry and Molecular Biophysics; Digestive System (Ingestion and
 Assimilation); Immune System (Chemical Coordination and Homeostasis)

IT Diseases
 gastroenteritis: digestive system disease; **rheumatoid**

arthritis: connective tissue disease, immune system disease, joint disease

IT Chemicals & Biochemicals
citrulline: urinary level; nitric oxide: production; nitrite: urinary level

IT Alternate Indexing
Arthritis, Rheumatoid (MeSH); Gastroenteritis (MeSH)

IT Methods & Equipment
spectrophotometry: measurement method

RN 14797-65-0 (NITRITE)
372-75-8 (**CITRULLINE**)
10102-43-9 (NITRIC OXIDE)

L91 ANSWER 15 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:130320 BIOSIS
DN PREV199900130320
TI Excitatory and inhibitory amino acid profiles of synovial fluids derived from patients with **arthritis**.
AU McNearney, T.; Speegle, D.; Lisse, N. Lawand J.; Westlund, K.
CS Univ. Texas Med. Branch, Galveston, TX USA
SO Journal of Investigative Medicine, (Feb., 1999) Vol. 47, No. 2, pp. 109A.
Meeting Info.: Meeting of the Southern Section of the American Federation for Medical Research New Orleans, Louisiana, USA February 18-20, 1999
American Federation for Medical Research
. ISSN: 1081-5589.

DT Conference
LA English
CC Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Endocrine System - General *17002
Nervous System - General; Methods *20501
Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520

BC Hominidae 86215
IT Major Concepts
Skeletal System (Movement and Support)

IT Parts, Structures, & Systems of Organisms
synovial fluid: skeletal system

IT Diseases
arthritis: joint disease; synovitis: joint disease

IT Chemicals & Biochemicals
arginine: metabolic control amino acid; aspartate [aspartic acid]: excitatory amino acid, synovial fluid, neurotransmitter;
citrulline: metabolic control amino acid; glutamate [glutamic acid]: excitatory amino acid, synovial fluid, neurotransmitter;
glycine: blood, inhibitory amino acid, synovial fluid, serum; serine: blood, synovial fluid, serum, inhibitory amino acid; threonine: metabolic control amino acid

IT Alternate Indexing
Arthritis (MeSH); Synovitis (MeSH)

IT Methods & Equipment
high performance liquid chromatography: analytical method

IT Miscellaneous Descriptors
joint inflammatory response; white blood cell count; Meeting Abstract; Meeting Poster

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae): patient
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 6899-03-2Q (ASPARTATE)
56-84-8Q (ASPARTATE)
56-84-8Q (ASPARTIC ACID)
617-45-8Q (ASPARTIC ACID)
11070-68-1 (GLUTAMATE)
56-86-0Q (GLUTAMIC ACID)
617-65-2Q (GLUTAMIC ACID)
56-45-1Q (SERINE)
302-84-1Q (SERINE)
72-19-5Q (THREONINE)
80-68-2Q (THREONINE)
372-75-8 (**CITRULLINE**)
74-79-3Q (**ARGININE**)
7200-25-1Q (**ARGININE**)

L91 ANSWER 16 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:474386 BIOSIS
DN PREV199800474386
TI Nitric oxide synthesis is increased in patients with systemic lupus
erythematosus.
AU Wanchu, A. (1); Khullar, M.; Deodhar, S. D.; Bambery, P.; Sud, A.
CS (1) Dep. Intern. Med., Postgrad. Inst. Med. Educ. Res., Chandigarh 160 012
India
SO Rheumatology International, (**Aug.**, 1998) Vol. 18, No. 2, pp.
41-43.
ISSN: 0172-8172.
DT Article
LA English
AB Nitric oxide (NO) is believed to have a role in the inflammatory process.
NO production was measured in 26 patients with systemic lupus
erythematosus (SLE) and 20 healthy volunteers, using
spectrophotometrically determined serum nitrite and **citrulline**
as surrogate markers. Both nitrite and **citrulline** levels were
significantly higher in patients with SLE than in controls ($P < 0.001$).
Twelve and 10 patients, respectively, with SLE had nitrite and
citrulline levels that were two standard deviations higher than
the mean level of controls. These patients had a significantly higher
measure of disease activity (SLE Disease Activity Index). These data show
that there is increased NO production in SLE and that it may serve as a
marker for disease activity.
CC Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
*18001
Biochemical Studies - General *10060
Metabolism - General Metabolism; Metabolic Pathways *13002
Endocrine System - General *17002
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae 86215
IT Major Concepts
Rheumatology (Human Medicine, Medical Sciences)
IT Diseases
systemic lupus erythematosus: connective tissue disease, immune system
disease
IT Chemicals & Biochemicals
citrulline: serum; nitric oxide: synthesis; nitrite: serum
IT Miscellaneous Descriptors
disease activity; inflammation
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae): patient

8-12, 1998 American College of Rheumatology
 . ISSN: 0004-3591.

DT Conference
 LA English
 CC **Immunology and Immunochemistry - General; Methods *34502**
 Genetics and Cytogenetics - Human *03508
 Biochemical Studies - General *10060
 General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annuals *00520
 BC Hominidae 86215
 IT Major Concepts
 Immune System (Chemical Coordination and Homeostasis)
 IT Diseases
 rheumatoid arthritis: connective tissue disease,
 immune system disease, joint disease
 IT Chemicals & Biochemicals
 anti-**citrulline**-containing peptides **antibodies:**
 serum
 IT Miscellaneous Descriptors
 rheumatoid arthritis related-HLA class II
 haplotypes; Meeting Abstract; Meeting Poster
 ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae): patient
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
 RN 372-75-8 (**CITRULLINE**)

L91 ANSWER 19 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1998:468693 BIOSIS
 DN PREV199800468693
 TI Epitope mapping of natural **filaggrin** leads to the identification
 of **rheumatoid arthritis**-immunoreactive epitopes
 containing **citrulline**.
 AU Union, Ann (1); Amerijckx, Liesbet (1); Raymackers, Jos (1); Dauwe,
 Martine (1); De Keyser, Filip; Veys, Eric; Meheus, Lydie (1)
 CS (1) Innogenetics N.V., Industriepark 7, 9052 Ghent Belgium
 SO Arthritis & Rheumatism, (**Sept., 1998**) Vol. 41, No. 9 SUPPL., pp.
 S84.
 Meeting Info.: 62nd National Scientific Meeting of the American College of
 Rheumatology and the 33rd National Scientific Meeting of the Association
 of Rheumatology Health Professionals San Diego, California, USA November
 8-12, 1998 American College of Rheumatology.
 . ISSN: 0004-3591.

DT Conference
 LA English
 CC Biochemical Studies - General *10060
 Immunology and Immunochemistry - General; Methods *34502
 General Biology - Symposia, Transactions and Proceedings of Conferences,
 Congresses, Review Annuals *00520
 IT Major Concepts
 Biochemistry and Molecular Biophysics
 IT Diseases
 rheumatoid arthritis: connective tissue disease,
 immune system disease, joint disease
 IT Chemicals & Biochemicals
 citrulline; filaggrin; rheumatoid
 arthritis-immunoreactive epitopes
 IT Methods & Equipment
 epitope mapping: analytical method
 IT Miscellaneous Descriptors
 Meeting Abstract; Meeting Poster

RN 372-75-8 (CITRULLINE)

L91 ANSWER 20 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:456752 BIOSIS

DN PREV199800456752

TI Design of isoform-selective inhibitors of nitric oxide synthase.

AU Babu, Boga Ramesh; Griffith, Owen W.

CS Dep. Biochem., Med. Coll. Wisconsin, Milwaukee, WI 53226 USA

SO Current Opinion in Chemical Biology, (Aug., 1998) Vol. 2, No. 4, pp. 491-500.

ISSN: 1367-5931.

DT General Review

LA English

CC Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

Biochemical Studies - General *10060

Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Biophysics - Molecular Properties and Macromolecules *10506

Enzymes - Physiological Studies *10808

IT Major Concepts

Enzymology (Biochemistry and Molecular Biophysics); Pharmacology

IT Diseases

arthritis: joint disease; diabetes: endocrine

disease/pancreas, metabolic disease; ischemic-reperfusion injury;

neurodegenerative diseases; septic shock: bacterial disease

IT Chemicals & Biochemicals

nitric oxide; nitric oxide synthase; nitric oxide synthase

isoform-selective inhibitors; ARL 17477; L-arginine:

oxidation; L-citrulline; N-5-(1-imino-3-butenyl)-L-ornithine;

S-(2-aminoethyl)isothioureia; 1400W

IT Miscellaneous Descriptors

pain

RN 125978-95-2 (NITRIC OXIDE SYNTHASE)

74-79-3 (L-ARGININE)

372-75-8 (L-CITRULLINE)

10102-43-9 (NITRIC OXIDE)

L91 ANSWER 21 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1998:274142 BIOSIS

DN PREV199800274142

TI Involvement of nitric oxide during phthalocyanine (Pc4) photodynamic therapy-mediated apoptosis.

AU Gupta, Sanjay; Ahmad, Nihal; Mukhtar, Hasan (1)

CS (1) Dep. Dermatol., Univ. Hosp. of Cleveland, Case Western Reserve Univ., 11100 Euclid Ave., Cleveland, OH 44106 USA

SO Cancer Research, (May 1, 1998) Vol. 58, No. 9, pp. 1785-1788.

ISSN: 0008-5472.

DT Article

LA English

AB Photodynamic therapy (PDT), a new treatment modality, uses a combination of photosensitizing agent and visible light for the therapy of many solid malignancies. The hallmark of PDT is intracellular oxidative stress mediated by reactive oxygen species, which, through a cascade of events, results in a cell kill that induces apoptosis in some cells. To better understand the mechanism of apoptosis, we hypothesized the role of nitric oxide (NO), which is considered to be involved in a variety of physiological and pathological processes, during PDT. The model photosensitizer we have been working with is a silicon-phthalocyanine compound termed Pc4. Here, we investigated the involvement of NO during Pc4 PDT in PDT of apoptosis-resistant radiation-induced fibrosarcoma (RIF-1) cells and in PDT of apoptosis-sensitive human epidermoid carcinoma (A431) cells. Pc4 PDT resulted in a rapid increase in nitrite production in A431 cells, starting as early as 15 s post-PDT, and showed a progressive increase up to 15 min post-PDT. This increase in nitrite

production was observed in cell lysates as well as in the cell culture medium. RIF-1 cells did not show an increase in nitrite production in either the cell lysates or the culture medium. At this time, a majority of the cells were viable. The Western blot analysis also showed a rapid increase in the expression of the constitutive form of NO synthase as early as 15 s post-PDT when compared to that of the controls. This response showed a dose dependency up to 5 min after Pc4 PDT. This observation was confirmed by a (3H)L-citrulline assay, which also showed a similar pattern for constitutive NO-synthase activity. RIF-1 cells did not show any change in protein expression or enzyme activity after the same treatment. These data, for the first time, demonstrate the generation of NO during PDT and suggest that it may be involved in PDT-mediated apoptosis. This may have relevance in improving the therapeutic efficacy of PDT using pharmacological modulators of NO or NO synthase.

- CC Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
 Cytology and Cytochemistry - Animal *02506
 Cytology and Cytochemistry - Human *02508
 Radiation - Radiation and Isotope Techniques *06504
 Radiation - Radiation Effects and Protective Measures *06506
 Metabolism - General Metabolism; Metabolic Pathways *13002
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
 Integumentary System - Pathology *18506
 Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
 Pharmacology - Integumentary System, Dental and Oral Biology *22020
 Neoplasms and Neoplastic Agents - Neoplastic Cell Lines *24005
 Neoplasms and Neoplastic Agents - Biochemistry *24006
 Biochemical Studies - General *10060
 Biochemical Studies - Minerals *10069
 External Effects - Light and Darkness *10604
 Pathology, General and Miscellaneous - Therapy *12512
 Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
 Neoplasms and Neoplastic Agents - Carcinogens and Carcinogenesis *24007
 Tissue Culture, Apparatus, Methods and Media *32500
- BC Hominidae 86215
 Muridae 86375
- IT Major Concepts
 Pharmacology; Tumor Biology
- IT Chemicals & Biochemicals
 nitric oxide: photodynamic therapy-mediated apoptosis involvement,
 tumor cell generation; silicon-phthalocyanine [Pc-4]: antineoplastic -
 drug, radiosensitizer - drug
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae:
 Rodentia, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 A-431 (Hominidae): human epidermoid carcinoma cell line, in-vitro model
 system, phthalocyanine photodynamic therapy-mediated apoptosis; RIF-1
 (Muridae): in-vitro model system, phthalocyanine photodynamic
 therapy-mediated apoptosis, mouse radiation-induced fibrosarcoma cell
 line
- ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman
 Vertebrates; Primates; Rodents; Vertebrates
- RN 10102-43-9 (NITRIC OXIDE)
 574-93-6 (PHTHALOCYANINE)
- L91 ANSWER 22 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1998:158398 BIOSIS
 DN PREV199800158398
 TI The modified **arginine** residue **citrulline** is the major
 constituent of epitopes recognized by **autoantibodies** in sera

- from **rheumatoid arthritis** patients.
- AU Schellekens, G. A. (1); De Jong, B. A. W. (1); Van Den Hoogen, F. H. J.;
Van De Putte, L. B. A.; Van Venrooij, W. J. (1)
- CS (1) Dep. Biochem., Univ. Nijmegen, Nijmegen Netherlands
- SO Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp.
S276.
- Meeting Info.: 61st National Scientific Meeting of the American College of
Rheumatology and the 32nd National Scientific Meeting of the Association
of Rheumatology Health Professionals Washington, DC, USA November 8-12,
1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.
- DT Conference
- LA English
- CC **Immunology and Immunochemistry - General; Methods *34502**
Biochemical Studies - General *10060
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
*18001
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
- BC Hominidae 86215
- IT Major Concepts
Immune System (Chemical Coordination and Homeostasis)
- IT Parts, Structures, & Systems of Organisms
serum: blood and lymphatics
- IT Diseases
rheumatoid arthritis: connective tissue disease,
immune system disease, joint disease
- IT Chemicals & Biochemicals
antikeratin **antibodies**; antiperinuclear factor;
citrullinated peptides; **citrulline**; **filaggrin**
; IgG **antibodies** [immunoglobulin G **antibodies**]
- IT Miscellaneous Descriptors
epitope recognition; Meeting Abstract; Meeting Poster
- ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
human (Hominidae)
- ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
- RN 74-79-3Q (**ARGININE**)
7200-25-1Q (**ARGININE**)
372-75-8 (**CITRULLINE**)
- L91 ANSWER 23 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
- AN 1998:94121 BIOSIS
- DN PREV199800094121
- TI **Citrulline** is an essential constituent of antigenic determinants
recognized by **rheumatoid arthritis**-specific
autoantibodies.
- AU Schellekens, Gerard A. (1); De Jong, Ben A. W.; Van Den Hoogen, Frank H.
J.; Van De Putte, Leo B. A.; Van Venrooij, Walther J.
- CS (1) Dep. Biochemistry, Univ. Nijmegen, PO Box 9101, 6500 HB Nijmegen
Netherlands
- SO Journal of Clinical Investigation, (Jan., 1998) Vol. 101, No. 1,
pp. 273-281.
ISSN: 0021-9738.
- DT Article
- LA English
- AB Only a few **autoantibodies** that are more or less specific for RA
have been described so far. The **rheumatoid** factor most often
tested for is not very specific for RA, while the more specific
antiperinuclear factor for several reasons is not routinely used as a
serological parameter. Here we show that **autoantibodies** reactive

with synthetic peptides containing the unusual amino acid **citrulline**, a posttranslationally modified **arginine** residue, are specifically present in the sera of RA patients. Using several **citrulline**-containing peptide variants in ELISA, **antibodies** could be detected in 76% of RA sera with a specificity of 96%. Sera showed a remarkable variety in the reactivity pattern towards different **citrulline**-containing peptides. Affinity-purified **antibodies** were shown to be positive in the immunofluorescence-based antiperinuclear factor test, and in the so-called antikeratin **antibody** test, and were reactive towards **filaggrin** extracted from human epidermis. The specific nature of these **antibodies** and the presence of these **antibodies** early in disease, even before other disease manifestations occur, are indicative for a possible role of **citrulline**-containing epitopes in the pathogenesis of RA.

- CC **Immunology and Immunochemistry - General; Methods *34502**
 Biochemical Studies - General *10060
 Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods *18001
- BC Hominidae 86215
- IT Major Concepts
 Immune System (Chemical Coordination and Homeostasis)
- IT Parts, Structures, & Systems of Organisms
 serum: blood and lymphatics
- IT Diseases
rheumatoid arthritis: connective tissue disease,
 immune system disease, joint disease
- IT Chemicals & Biochemicals
 antikeratin **antibodies**; antiperinuclear factor; autoantigens;
citrulline; **filaggrin**; **rheumatoid**
arthritis-specific autoantibodies; **rheumatoid**
 factor
- ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 human (Hominidae): patient
- ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates
- RN 372-75-8 (**CITRULLINE**)
- L91 ANSWER 24 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1997:183441 BIOSIS
 DN PREV199799482644
 TI Inducible nitric oxide synthase and cyclooxygenase are expressed in human-TNF-alpha transgenic mice which develop **arthritis** spontaneously.
- AU Platts, L. A. M. (1); Haralambous, S.; Hukkanen, M. V. J. (1); Gross, S. S.; Maclouf, J.; Kollias, G.; Polak, J. M. (1)
 (1) Dep. Histochem., Royal Postgrad. Med. Sch., London W12 ONN UK
- CS Journal of Pathology, (1997) Vol. 181, No. SUPPL., pp. 42A.
- SO Meeting Info.: 174th Meeting of the Pathological Society of Great Britain and Ireland London, England, UK January 8-10, 1997
 ISSN: 0022-3417.
- DT Conference; Abstract
- LA English
- CC Cytology and Cytochemistry - Animal *02506
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
 Endocrine System - General *17002

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology***18006**

BC Muridae *86375

IT Major Concepts

Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Pathology; Skeletal System (Movement and Support)

IT Chemicals & Biochemicals

NITRIC OXIDE SYNTHASE; CYCLOOXYGENASE; TETRAHYDROBIOPTERIN;
ARGININOSUCCINATE SYNTHETASE; **CITRULLINE**; NITRIC
 OXIDE; 6-KETO-PROSTAGLANDIN-F1-ALPHA

IT Miscellaneous Descriptors

ARGININOSUCCINATE SYNTHETASE; CHONDROCYTES; CHRONIC
ARTHRITIS; **CITRULLINE**; CYCLOOXYGENASE 2; ENDOCRINE
 SYSTEM; ENZYMOLOGY; EXPRESSION; GUANIDINE TRIPHOSPHATE CYCLOHYDROLASE;
 HUMAN TUMOR NECROSIS FACTOR-ALPHA TRANSGENE; HUMAN-TUMOR NECROSIS
 FACTOR-ALPHA TRANSGENETIC; INDUCIBLE NITRIC OXIDE SYNTHASE;
 INFLAMMATORY CYTOKINES; JOINT DISEASE; NITRIC OXIDE; PRODUCTION;
 PROSTAGLANDIN PGE2; SKELETAL SYSTEM; SYNOVIAL-CARTILAGE JUNCTION;
 SYNTHESIS; TETRAHYDROBIOPTERIN; 3'-MODIFIED; 6-KETO-PROSTAGLANDIN-F1-
 ALPHA

ORGN Super Taxa

Muridae; Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

mouse (Muridae)

ORGN Organism Superterms

animals; chordates; mammals; nonhuman mammals; nonhuman vertebrates;
 rodents; vertebrates

RN 125978-95-2 (NITRIC OXIDE SYNTHASE)

39391-18-9 (CYCLOOXYGENASE)

17528-72-2 (TETRAHYDROBIOPTERIN)

9023-58-9 (**ARGININOSUCCINATE** SYNTHETASE)372-75-8 (**CITRULLINE**)

10102-43-9 (NITRIC OXIDE)

58962-34-8 (6-KETO-PROSTAGLANDIN-F1-ALPHA)

L91 ANSWER 25 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1997:151563 BIOSIS

DN PREV199799450766

TI Nitric oxide production by superficial and deep articular chondrocytes.

AU Hayashi, Takeshi; Abe, Etsuko; Yamate, Tomoo; Taguchi, Yasuto; Jasin, Hugo E. (1)

CS (1) Div. Rheumatology, Mail Slot 509, Univ. Arkansas Med. Sci., 4301 West Markham, Little Rock, AR 72205 USA

SO Arthritis & Rheumatism, (1997) Vol. 40, No. 2, pp. 261-269.

ISSN: 0004-3591.

DT Article

LA English

AB Objective. Chondrocytes have been shown to produce large amounts of nitric oxide (NO) when appropriately stimulated with proinflammatory cytokines or bacterial lipopolysaccharide (LPS). In view of recent observations underscoring profound phenotypic differences between superficial and deep articular chondrocytes, these studies investigated NO production, inducible NO synthase (iNOS) activity, and messenger RNA (mRNA) expression of superficial and deep cartilage explants and cells. Methods. Superficial and deep bovine and human articular cartilage explants and isolated bovine chondrocytes were cultured in the presence of stimulating cytokines or LPS. NO was measured by the Griess reagent. Inducible NOS activity was quantitated by conversion of L-14C-**arginine** to L-14C-**citrulline**. Inducible NOS mRNA expression was quantitated by reverse transcription-polymerase chain reaction (RT-PCR) and in situ hybridization. Results. Superficial bovine cartilage explants stimulated

with interleukin-1-alpha, LPS, or tumor necrosis factor α for 24 and 48 hours produced significantly more NO than did deep explants with all stimulants and at both times. Similar results were obtained with stimulated isolated superficial and deep cells. NO synthase activity, measured by the conversion of L-14 C-**arginine** to L-14C-**citrulline**, paralleled NO production. Comparable results were obtained using explants from a normal human donor. Semiquantitation of iNOS mRNA by RT-PCR showed significantly larger amounts of PCR products in superficial cells and superficial explants. These results were confirmed by in situ hybridization of explants and isolated cells. Conclusion. Increased NO production at the cartilage surface-synovial fluid interface may play an important role in the modulation of cartilage damage in inflammatory **arthritis**.

- CC Cytology and Cytochemistry - Animal *02506
 Cytology and Cytochemistry - Human *02508
 Enzymes - Physiological Studies *10808
 Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
 Cardiovascular System - Physiology and Biochemistry *14504
 Endocrine System - Neuroendocrinology *17020
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
 Nervous System - Physiology and Biochemistry *20504
- BC Bovidae 85715
 Hominidae *86215
- IT Major Concepts
 Cardiovascular System (Transport and Circulation); Cell Biology;
 Endocrine System (Chemical Coordination and Homeostasis); Enzymology
 (Biochemistry and Molecular Biophysics); Metabolism; Nervous System
 (Neural Coordination); Pathology; Skeletal System (Movement and Support)
- IT Chemicals & Biochemicals
 NITRIC OXIDE; NITRIC OXIDE SYNTHASE
- IT Miscellaneous Descriptors
 ACTIVITY; **ARTHRITIS**; ARTICULAR CHONDROCYTE; CARTILAGE DAMAGE
 MODULATION; CARTILAGE SURFACE-SYNOVIAL FLUID INTERFACE; DEEP;
 EXPRESSION; INDUCIBLE NITRIC OXIDE SYNTHASE; JOINT DISEASE; MESSENGER
 RNA; NITRIC OXIDE; PRODUCTION; SKELETAL SYSTEM; SUPERFICIAL
- ORGN Super Taxa
 Bovidae: Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia;
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
- ORGN Organism Name
 bovine (Bovidae); human (Hominidae)
- ORGN Organism Superterms
 animals; artiodactyls; chordates; humans; mammals; nonhuman mammals;
 nonhuman vertebrates; primates; vertebrates
- RN 10102-43-9 (NITRIC OXIDE)
 125978-95-2 (NITRIC OXIDE SYNTHASE)
- L91 ANSWER 26 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1996:565642 BIOSIS
 DN PREV199799294998
 TI Plasma reactive nitrogen intermediate levels in patients with clinically active **rheumatoid arthritis**.
 AU Wanchu, A. (1); Agnihotri, N.; Deodhar, S. D.; Ganguly, N. K.
 CS (1) Dep. Intern. Med., Postgrad. Inst. Med. Educ. Res., Chandigarh 160012 India
 SO Indian Journal of Medical Research, (1996) Vol. 104, No. OCT., pp. 263-268.

ISSN: 0971-5916.

DT Article

LA English

AB We studied reactive nitrogen intermediate levels in 31 patients with active **rheumatoid arthritis** (RA) taking indomethacin and 20 healthy controls using nitrite and **citrulline** levels, measured by spectrophotometry, as markers. Twenty patients with RA were followed up after 4 and 8 wk of treatment with additional therapy in the form of methotrexate. Mean. nitrite levels in 31 patients were 0.94 ± 0.41 $\mu\text{mol/ml}$ and 20 controls it was 1.18 ± 0.99 . After treatment with methotrexate for 4 and 8 wk the levels were 0.9 ± 0.45 and 1.25 ± 1.15 $\mu\text{mol/ml}$, respectively. Mean **citrulline** levels in all patients was 1.68 ± 0.11 and controls was 1.39 ± 0.6 $\mu\text{mol/ml}$. Following therapy with methotrexate for 4 and 8 wk the levels were 1.40 ± 0.49 and 1.40 ± 0.51 $\mu\text{mol/ml}$, respectively. It is possible that serum levels of these products may not reflect alterations in the synovial fluid levels. Alternatively, whatever lowering may have been achieved by the anti-inflammatory effect of the therapy may have been countered by drug derived free radicals.

CC Biochemical Studies - General 10060
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biochemical Studies - Minerals 10069
 Biophysics - Molecular Properties and Macromolecules 10506
 Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease 12508
 Pathology, General and Miscellaneous - Therapy 12512
 Metabolism - Minerals *13010
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies 15002
 Blood, Blood-Forming Organs and Body Fluids - Other Body Fluids 15010
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
 Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
 Pharmacology - Clinical Pharmacology *22005
 Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
 Pharmacology - Immunological Processes and Allergy 22018
 Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Hominidae *86215

IT Major Concepts
 Metabolism; Pharmacology; Skeletal System (Movement and Support)

IT Chemicals & Biochemicals
 NITROGEN; INDOMETHACIN; METHOTREXATE; NITRITE; **CITRULLINE**

IT Miscellaneous Descriptors
ANTIARTHRITIC-DRUG; CITRULLINE; CONNECTIVE TISSUE DISEASE; DRUG TREATMENT; IMMUNE SYSTEM DISEASE; INDOMETHACIN; JOINT DISEASE; METHOTREXATE; NITRITE; ORTHOPEDICS; PATIENT; PHARMACOLOGY; PLASMA LEVEL; REACTIVE NITROGEN INTERMEDIATE; RHEUMATOID ARTHRITIS

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae)

ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates

RN 7727-37-9 (NITROGEN)
 53-86-1 (INDOMETHACIN)
 59-05-2 (METHOTREXATE)
 14797-65-0 (NITRITE)
 372-75-8 (**CITRULLINE**)

L91 ANSWER 27 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1996:365979 BIOSIS
 DN PREV199699088335
 TI Hyperornithinemia-hyperammonemia-**homocitrullinuria**
 (HHH)-syndrome: Ultrastructural changes of mitochondria in cultured dermal fibroblasts of three patients.
 AU Haust, M. Daria (1); Dewar, R. A.; Gatfield, D. P.; Gordon, B. A.
 CS (1) Dep. Pathol., Fac. Med., Univ. Western Ont., London, ON N6A 5C1 Canada
 SO Pathology Research and Practice, (1996) Vol. 192, No. 3, pp. 271-280.
 ISSN: 0344-0338.
 DT Article
 LA English
 AB Mitochondria of fibroblasts cultured from the skin obtained at biopsy from three patients with the hyperornithinemia-hyperammonemia-**homocitrullinuria** (HHH)-syndrome, one of the autosomal recessive, heritable urea cycle disorders, were studied with appropriate controls ultrastructurally. The patients were two severely retarded 10- and 12-year-old boys, and a 22-year-old sister of the former whose mental status was at the low normal range; she never had motor impairments or seizures. The mitochondria, similar in all three patients, were increased in number, very long, branching and/or "looping," and tortuous. "Spurs" or "buddings" extended from their lateral surfaces and the terminal segments were often bulbous. Other unusual configurations were also present. In addition, giant forms with large diameter contained innumerable closely-packed and parallel cristae which traversed the entire width of these mitochondria; at times they assumed a "whirled" pattern. The mitochondrial matrix was usually of high electron density. These changes were not a feature of fibroblastic mitochondria of controls. Several changes resembled those of hepatic mitochondria in this disorder. All features are interpreted as an attempt at expanding the mitochondrial volume (via structural substratum) to compensate for the metabolic incompetence of these organelles (a block in transmembranous transfer of ornithine from hyaloplasm into mitochondria for conversion to **citrulline**).
 CC Cytology and Cytochemistry - Human *02508
 Genetics and Cytogenetics - Human *03508
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Enzymes - Physiological Studies *10808
 Metabolism - Proteins, Peptides and Amino Acids *13012
 Metabolism - Metabolic Disorders *13020
 Digestive System - Anatomy *14002
 Digestive System - Physiology and Biochemistry *14004
 Digestive System - Pathology *14006
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Anatomy *18002
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Physiology and Biochemistry *18004
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
 Integumentary System - Anatomy *18502
 Integumentary System - Physiology and Biochemistry *18504
 Integumentary System - Pathology *18506
 Developmental Biology - Embryology - Pathological *25503
 In Vitro Studies, Cellular and Subcellular *32600
 BC Hominidae *86215
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology; Dermatology (Human Medicine, Medical Sciences); Development; Digestive System (Ingestion and Assimilation); Enzymology (Biochemistry and Molecular Biophysics); Gastroenterology (Human Medicine, Medical Sciences); Genetics; Integumentary System (Chemical Coordination and Homeostasis); Metabolism; Skeletal System (Movement and Support)
 IT Chemicals & Biochemicals
 UREA

IT Miscellaneous Descriptors
 ADULT; CELL BIOLOGY; CELL CULTURE; CHEMICAL COORDINATION AND
 HOMEOSTASIS/INTEGUMENTARY SYSTEM; DERMAL FIBROBLASTS; FEMALE; GENETIC
 DISEASE; HEPATIC MITOCHONDRIA; HERITABLE UREA CYCLE DISORDER; HHH
 SYNDROME; HYPERORNITHINEMIA-HYPERAMMONEMIA-HOMOCITRULLINURIA
 SYNDROME; MALE; METABOLIC DISEASE; MITOCHONDRIA ULTRASTRUCTURAL
 CHANGES; MOVEMENT AND SUPPORT/SKELETAL SYSTEM; PATIENT; PREADOLESCENT

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae)

ORGN Organism Superterms
 animals; chordates; humans; mammals; primates; vertebrates

RN 57-13-6 (UREA)

L91 ANSWER 28 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1996:267942 BIOSIS
 DN PREV199698824071
 TI Database cloning human DELTA-1-pyrroline-5-carboxylate synthetase (P5CS)
 cDNA: A bifunctional enzyme catalyzing the first 2 steps in proline
 biosynthesis.

AU Aral, Bernard (1); Schlenzig, Jan-Sebastian; Liu, Guang; Kamoun, Pierre
 CS (1) Laboratoire de Biochimie Medicale B, Centre National de la Recherche
 Scientifique, URA 1335, Hopital Necker-Enfants-Malades, 149 rue de Sevres,
 75015 Paris France

SO Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie,
 (1996) Vol. 319, No. 3, pp. 171-178.
 ISSN: 0764-4469.

DT Article
 LA English
 SL English; French

AB DELTA-1-pyrroline-5-carboxylate synthetase (P5CS) catalyzes the ATP and
 the NAD(P)H-dependent conversion of L-glutamate to glutamic γ -semialdehyde
 (GSA) which is the metabolic precursor for proline biosynthesis. We cloned
 a human P5CS cDNA by database cloning strategy and sequenced 2,907 bp from
 this cDNA which has a closed open reading frame (ORF) of 2,385 bp coding
 for a polypeptide of 795 amino acid residues. This cDNA, as its plant
 counterpart, encodes a bifunctional enzyme, with both gamma-glutamyl
 kinase (gamma-GA) and gamma-glutamyl phosphate reductase (gamma-GPR)
 activities that catalyzes the first 2 steps in proline biosynthesis and it
 hybridizes to a 4.5 kb mRNA from various tissues. A human genetic disease
 caused by a deficient P5CS has been recognized. The phenotypic features
 for deficiency of P5CS include joint hyperlaxity, skin hyperelasticity,
 cataract and mental retardation with hyperammonemia and low plasma levels
 of proline, **citrulline** and ornithine.

CC Genetics and Cytogenetics - Human *03508
 Comparative Biochemistry, General *10010
 Biochemical Studies - General 10060
 Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
 Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Enzymes - Chemical and Physical *10806
 Enzymes - Physiological Studies *10808
 Metabolism - General Metabolism; Metabolic Pathways *13002
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**
 Integumentary System - Pathology *18506
 Sense Organs, Associated Structures and Functions - Pathology *20006
 Nervous System - Pathology *20506
 Psychiatry - Mental Retardation *21006

BC Hominidae *86215

IT Major Concepts
 Biochemistry and Molecular Biophysics; Dermatology (Human Medicine,

Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Genetics; Metabolism; Neurology (Human Medicine, Medical Sciences); Psychiatry (Human Medicine, Medical Sciences); Sense Organs (Sensory Reception); Skeletal System (Movement and Support)

IT Chemicals & Biochemicals
PROLINE; ATP; **CITRULLINE**; ORNITHINE; GAMMA-GLUTAMYL KINASE;
GAMMA-GLUTAMYL PHOSPHATE REDUCTASE

IT Sequence Data
amino acid sequence; molecular sequence data; nucleotide sequence;
EMBL-X94453

IT Miscellaneous Descriptors
ATP; CATARACT; **CITRULLINE**; CLOSED OPEN READING FRAME;
COMPLEMENTARY DNA; GAMMA-GLUTAMYL KINASE; GAMMA-GLUTAMYL PHOSPHATE
REDUCTASE; GENETIC DISEASE; HYPERAMMONEMIA; JOINT HYPERLAXITY; MENTAL
RETARDATION; MESSENGER RNA; ORNITHINE; SKIN HYPERELASTICITY

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Hominidae (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

RN 147-85-3 (PROLINE)
56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)
372-75-8 (**CITRULLINE**)
70-26-8 (ORNITHINE)
54596-30-4 (GAMMA-GLUTAMYL KINASE)
54596-29-1 (GAMMA-GLUTAMYL PHOSPHATE REDUCTASE)

L91 ANSWER 29 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1993:365710 BIOSIS
DN PREV199396051385
TI Role of haematological, pulmonary and renal complications in the long-term
prognosis of patients with lysinuric protein intolerance.
AU Dirocco, M. (1); Garibotto, G.; Rossi, G. A.; Caruso, U.; Taccone, A.;
Picco, P.; Borrone, C.
CS (1) II Div. Pediatria, Ist. G. Gaslini, Largo G. Gaslini 5, I-16148 Genova
Italy
SO European Journal of Pediatrics, (1993) Vol. 152, No. 5, pp. 437-440.
ISSN: 0340-6199.
DT Article
LA English
AB Three patients with lysinuric protein intolerance are reported. The first
patient displayed severe haemolytic anaemia, bone marrow
erythroblastophagocytosis, renal tubular disease and interstitial lung
disease. Despite treatment with **citrulline** and low-protein diet,
this child died at the age of 18 months. The second patient is now 24
years old and has chronic interstitial lung disease and focal renal
glomerulosclerosis. The third patient, now 5 years old, has severe chronic
interstitial lung disease. A 6-month treatment with prednisone was
ineffective in the second and third patients.

CC Genetics and Cytogenetics - Human *03508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Metabolic Disorders *13020
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and
Reticuloendothelial Pathologies *15006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and
Reticuloendothelial System *15008
Urinary System and External Secretions - Pathology *15506

Respiratory System - Pathology *16006

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006

Pediatrics *25000

Developmental Biology - Embryology - Pathological *25503

Immunology and Immunochemistry - Immunohematology, Blood Groups

*34506

Immunology and Immunochemistry - Immunopathology, Tissue Immunology

*34508

BC Hominidae *86215

IT Major Concepts

Blood and Lymphatics (Transport and Circulation); Clinical Immunology (Human Medicine, Medical Sciences); Development; Enzymology (Biochemistry and Molecular Biophysics); Genetics; Hematology (Human Medicine, Medical Sciences); Immune System (Chemical Coordination and Homeostasis); Metabolism; Pediatrics (Human Medicine, Medical Sciences); Pulmonary Medicine (Human Medicine, Medical Sciences); Skeletal System (Movement and Support); Urology (Human Medicine, Medical Sciences)

IT Miscellaneous Descriptors

BIOTIN SUPPLEMENTATION; LACTIC ACIDOSIS; LYMPHOCYTE; MITOCHONDRIA; MULTIPLE CARBOXYLASE DEFICIENCY; ORGANIC ACIDURIA

ORGN Super Taxa

Hominidae; Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

animals; chordates; humans; mammals; primates; vertebrates

L91 ANSWER 30 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1991:49503 BIOSIS

DN BA91:27784

TI INHERITED HYPERACTIVITY OF L **ARGININE** SYNTHESIS IN GAMMA POSITIVE B LYMPHOCYTES OF SYSTEMIC AUTOIMMUNE MRL MICE.

AU SUGIMURA K; WADA Y; KIMURA T; OHNO T; KOBAYASHI S; AZUMA I

CS INST. IMMUNOL. SCI., HOKKAIDO UNIV., SAPPORO 060, JPN.

SO INT IMMUNOL, (1990) 2 (11), 1033-1038.

CODEN: INIMEN.

FS BA; OLD

LA English

AB The hyperactivation of B lymphocytes of MRL mice, which are an animal model for human systemic lupus erythematosus (SLE), is characterized as the preferential propagation of .gamma.+ B lymphocytes and IgG overproduction followed by aging. Little is known about the molecular mechanisms, although the involvement of cytokines has been extensively investigated. Here we now show that .gamma.-committed B lymphocytes selectively exhibit a highly elevated L-**citrulline** metabolism while .mu. or .alpha.-committed B lymphocytes show normal level in autoimmune MRL mice. L-**Arginine** proportionally supports the lymphocyte proliferation and **antibody** production in a concentration-dependent fashion (.apprx. 100 .mu.M). However, normal murine lymphocytes show an extremely low activity of **citrulline** metabolism, which converts L-**citrulline** to L-**arginine**. Thus, these results suggest tht the overexpression of elevated **citrulline** metabolism is associated with .gamma. chain expression, and this elevation may enable .gamma.-committed B lymphocytes to preferentially propagate and overproduce IgG compared with .mu. or .alpha.-committed B lymphocytes.

CC Cytology and Cytochemistry - Animal *02506

Genetics and Cytogenetics - Animal *03506

Biochemical Studies - Proteins, Peptides and Amino Acids *10064

Biophysics - Molecular Properties and Macromolecules *10506

Pathology, General and Miscellaneous - Inflammation and Inflammatory

Disease *12508
Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies
*15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and
Reticuloendothelial System *15008
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006
Gerontology *24500
Developmental Biology - Embryology - Morphogenesis, General *25508
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508
BC Muridae 86375
IT Miscellaneous Descriptors
SYSTEMIC LUPUS ERYTHEMATOSUS AGING IMMUNOGLOBULIN G OVERPRODUCTION L
CITRULLINE
RN 74-79-3 (L ARGININE)
372-75-8 (L CITRULLINE)

L91 ANSWER 31 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1989:253814 BIOSIS
DN BR36:121038
TI LYSINURIC PROTEIN INTOLERANCE INTEREST OF OROTIC ACIDURIA TO ADJUST
CITRULLINE THERAPY.
AU DE PARSCAU L; VIANEY-LIAUD C; HERMIER M; DIVRY P; GIUBAID P
CS L'UNITE D'ETUDES DES METABOLIQUES, HOP. DEBROUSSE, 29, RUE SOEUR-BOUVIER,
69322 LYON CEDEX 05.
SO Arch. Fr. Pediatr., (1988) 45 (10), 809-812.
CODEN: AFPEAM. ISSN: 0003-9764.
FS BR; OLD
LA French
CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Chordate Body Regions - Extremities 11318
Pathology, General and Miscellaneous - Diagnostic *12504
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - Proteins, Peptides and Amino Acids *13012
Metabolism - Metabolic Disorders *13020
Nutrition - Prophylactic and Therapeutic Diets *13218
Nutrition - Proteins, Peptides and Amino Acids *13224
Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
18001
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006
Pediatrics *25000
Developmental Biology - Embryology - Morphogenesis, General *25508
BC Hominidae 86215
IT Miscellaneous Descriptors
CHILD AMINO ACID METABOLISM GROWTH FAILURE VERTEBRAL OSTEOPOROSIS
PROTEIN AVERSION DIGITAL HIPPOCRATISM DIET THERAPY
RN 372-75-8 (CITRULLINE)

L91 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1988:231589 BIOSIS
DN BR34:114109
TI STUDIES ON THE INCREASE IN SERUM CONCENTRATIONS OF UREA CYCLE AMINO ACIDS
AMONG SUBJECTS EXPOSED TO CADMIUM.
AU NISHINO H; SHIROISHI K; KAGAMIMORI S; NARUSE Y; WATANABE M
CS TOYAMA INST. HEALTH, 2630 SUGITANI, TOYAMA-SHI, TOYAMA 930-01, JPN.
SO Bull. Environ. Contam. Toxicol., (1988) 40 (4), 553-560.
CODEN: BECTA6. ISSN: 0007-4861.
FS BR; OLD
LA English
CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Minerals 10069
 Metabolism - Proteins, Peptides and Amino Acids *13012
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies
***15002**
 Urinary System and External Secretions - Physiology and Biochemistry
 *15504
 Urinary System and External Secretions - Pathology *15506
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
18006

Toxicology - Environmental and Industrial Toxicology *22506

BC Hominidae 86215

IT Miscellaneous Descriptors

HUMAN METALS ITAI-ITAI DISEASE KINETICS **CITRULLINE**

ARGININE ORNITHINE

RN 57-13-6 (UREA)

372-75-8 (**CITRULLINE**)

7440-43-9 (CADMIUM)

70-26-8Q, 7006-33-9Q (ORNITHINE)

74-79-3Q, 7004-12-8Q (**ARGININE**)

L91 ANSWER 33 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1986:378444 BIOSIS

DN BA82:73420

TI PLASMA AMINO-ACIDS IN **RHEUMATOID ARTHRITIS**.

AU TRANG L E; FURST P; ODEBACK A-C; LOVGREN O

CS RHEUMATOL. METABOLIC RES. LAB., ST. ERIK'S HOSP., S-112 82 STOCKHOLM, SWEDEN.

SO SCAND J RHEUMATOL, (1985 (RECD 1986)) 14 (4), 393-402.

CODEN: SJRHAT. ISSN: 0300-9742.

FS BA; OLD

LA English

AB Plasma amino acid concentrations have been investigated in 12 female patients with **rheumatoid arthritis** (RA), who were hospitalized for two 14-day periods, one of which included 7 days of total fasting, whereas the other served as control period with normal food intake. All medical treatment was stopped on admission to the hospital. Plasma amino acid levels were repeatedly determined during both periods. Another group, consisting of 8 healthy volunteers, also underwent total fasting, for 6 days. The response to food deprivation with regard to plasma amino acid levels was compared with that in the RA patients. The results obtained from the control period were compared with those derived from age and sex matched healthy controls. RA disease was not characterized by a typical amino acid pattern. Major increases were seen in the concentration of taurine, aspartate, glutamate, glycine, l-methyl histidine, isoleucine and **arginine**. Rather smaller yet significant elevations could be observed in the levels of cysteine, threonine, serine, **citrulline**, methionine and leucine. The only amino acid to show a lowered concentration was .alpha.-aminobutyrate. Most of the alterations induced by fasting were similar to those in healthy volunteers. An exception was the levels of taurine, which evidenced in RA patients a further increase during starvation, not observed in healthy volunteers, and valine which exhibited, a smaller increment than that apparent in healthy controls. The increase in sulphur-containing amino acid smight be interpreted as a sign of an enhanced glutathione (GSH) catabolism, whereas the differing metabolic behaviour of branched chain amino acids (BCAA) suggests a specific reaction of valine in RA disease, similar to that in other catabolic diseases.

CC Clinical Biochemistry; General Methods and Applications *10006

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508

Pathology, General and Miscellaneous - Therapy *12512

Metabolism - Proteins, Peptides and Amino Acids *13012

Nutrition - General Dietary Studies *13214
Nutrition - Prophylactic and Therapeutic Diets *13218
Blood, Blood-Forming Organs and Body Fluids - Blood and Lymph Studies
***15002**

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
***34508**

BC Hominidae 86215

IT Miscellaneous Descriptors
HUMAN FASTING THERAPEUTIC DIET

L91 ANSWER 34 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1985:73668 BIOSIS

DN BR28:73668

TI LYSINURIC PROTEIN INTOLERANCE PRESENTING AS CHILDHOOD OSTEOPOROSIS
CLINICAL AND SKELETAL RESPONSE TO **CITRULLINE** THERAPY.

AU CARPENTER T O; LEVY H L; HOLTROP M E; SHIH V E; ANAST C S

CS DIV. ENDOCRINOLOGY, CHILDREN'S HOSPITAL, BOSTON, MA 02115.

SO N. Engl. J. Med., (1985) 312 (5), 290-294.

CODEN: NEJMAG. ISSN: 0028-4793.

FS BR; OLD

LA English

CC Genetics and Cytogenetics - Human *03508

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biochemical Studies - Minerals 10069

Enzymes - Chemical and Physical *10806

Enzymes - Physiological Studies *10808

Pathology, General and Miscellaneous - Therapy *12512

Metabolism - Minerals *13010

Metabolism - Proteins, Peptides and Amino Acids *13012

Nutrition - Prophylactic and Therapeutic Diets *13218

Nutrition - Proteins, Peptides and Amino Acids *13224

Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**

Pharmacology - Clinical Pharmacology 22005

BC Hominidae 86215

IT Miscellaneous Descriptors

METABOLIC-DRUG AUTOSOMAL RECESSIVE DEFICIT ORNITHINE DECARBAMYLASE BONE
DEMINERALIZATION

RN 372-75-8 (**CITRULLINE**)

70-26-8Q, 7006-33-9Q (ORNITHINE).

L91 ANSWER 35 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1984:101703 BIOSIS

DN BR27:18195

TI **ARGININE** AND THE GROWTH OF NORMAL AND NEOPLASTIC CELLS.

AU CLARK J E; MILNER J A

CS DEP. FOOD SCI., UNIV. ILL., URBANA, IL 61801.

SO 68TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR
EXPERIMENTAL BIOLOGY, ST. LOUIS, MO., USA, APR. 1-6, 1984 FED PROC. (1984)
43 (3), ABSTRACT 658.

CODEN: FEPR7. ISSN: 0014-9446.

DT Conference

FS BR; OLD

LA English

CC General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals 00520

Cytology and Cytochemistry - Animal *02506

Biochemical Studies - General 10060

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Pathology, General and Miscellaneous - Necrosis 12510

Metabolism - Proteins, Peptides and Amino Acids *13012

Bones, Joints, Fasciae, Connective and Adipose Tissue - General; Methods
18001

**Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
18006**

Integumentary System - Pathology 18506

Pharmacology - Drug Metabolism; Metabolic Stimulators *22003

Neoplasms and Neoplastic Agents - Neoplastic Cell Lines 24005

Neoplasms and Neoplastic Agents - Biochemistry *24006

Neoplasms and Neoplastic Agents - Carcinogens and Carcinogenesis 24007

Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008

Developmental Biology - Embryology - Experimental 25504

Tissue Culture, Apparatus, Methods and Media 32500

Virology - Animal Host Viruses 33506

BC Papovaviridae 02226

Bovidae 85715

Muridae 86375

IT Miscellaneous Descriptors

ABSTRACT MOUSE EMBRYONIC FIBROBLAST 3T3 CELLS 3T3 SV-40 TRANSFORMED 3T3

CELLS FETAL BOVINE SERUM ANTINEOPLASTIC-DRUG AMINO-ACID PROTEIN GROWTH

INHIBITION ORNITHINE UREA **CITRULLINE**

RN 57-13-6 (UREA)

372-75-8 (**CITRULLINE**)

70-26-8Q, 7006-33-9Q (ORNITHINE)

74-79-3Q, 7004-12-8Q (**ARGININE**)

L91 ANSWER 36 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1981:116420 BIOSIS

DN BR21:51416

TI DOES **ARGININE** DEIMINASE CATALYZE A **CITRULLINE** WATER
EXCHANGE REACTION.

AU PAIGE M R; FAHRNEY D E

CS COLORADO STATE UNIV., FORT COLLINS, CO. 80523.

SO 72ND ANNUAL MEETING OF THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, ST.

LOUIS, MO., USA, MAY 31-JUNE 4, 1981. FED PROC. (1981) 40 (6), 1866.

CODEN: FEPR7. ISSN: 0014-9446.

DT Conference

FS BR; OLD

LA English

CC General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals 00520

Radiation - Radiation and Isotope Techniques. 06504

Biochemical Methods - Proteins, Peptides and Amino Acids 10054

Biochemical Studies - General 10060

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Enzymes - Methods 10804

Enzymes - Chemical and Physical *10806

Enzymes - Physiological Studies *10808

Metabolism - Proteins, Peptides and Amino Acids. *13012

Physiology and Biochemistry of Bacteria *31000

Microbiological Apparatus, Methods and Media 32000

BC Mycoplasmataceae 09112

IT Miscellaneous Descriptors

ABSTRACT MYCOPLASMA-**ARTHRITIDIS** MECHANISM AMMONIA RELEASE

CARBON-13 NMR

RN 7664-41-7 (AMMONIA)

9027-98-9 (**ARGININE** DEIMINASE)

14762-74-4 (CARBON-13)

L91 ANSWER 37 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1980:267167 BIOSIS

DN BA70:59663

TI THE EFFECT OF SELECTED AMINO-ACIDS ON GELATIN INDUCED INFLAMMATION IN
ADULT MALE MICE.

- AU MEYERS B E; MOONKA D K; DAVIS R H
CS DEP. PHYSIOL. SCI., PA. COLL. PODIATR. MED., PHILADELPHIA, PA. 19107, USA.
SO INFLAMMATION, (1979) 3 (3), 225-234.
CODEN: INFLD4. ISSN: 0360-3997.
- FS BA; OLD
LA English
AB Certain amino acids may exhibit antiinflammatory activity. The inhibitory effect of various amino acids on gelatin-induced abdominal inflammation in mice was evaluated using peritoneal fluid cytology as the diagnostic tool. The L-amino acids tested were tryptophan, phenylalanine, alanine, cystine, hydroxyproline, tyrosine, **citrulline**, leucine, and valine. Hydrocortisone was used as an antiphlogistic steroid control. Tryptophan, phenylalanine, alanine, cystine, hydroxyproline and tyrosine all significantly decreased the inflammation. **Citrulline** and valine exhibited strong antiinflammatory responses. Based on these results, 3 related dipeptides were also screened: L-valyl-L-alanine, L-valyl-L-tryptophan and L-tyrosyl-L-valine. Valyl alanine produced a strong antiinflammatory effect. In a final test, the combination of the steroid, hydrocortisone, and the amino acid, cystine, was screened for a synergistic effect. The combined treatment inhibited the gelatin-induced inflammation more than either the amino acid or the steroid administered alone.
- CC Microscopy Techniques - Cytology and Cytochemistry 01054
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Sterols and Steroids 10067
Chordate Body Regions - Abdomen 11314
Pathology, General and Miscellaneous - Diagnostic 12504
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
 Blood, Blood-Forming Organs and Body Fluids - Other Body Fluids
 15010
 Endocrine System - Adrenals 17004
 Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
 ***18006**
 Coelomic Membranes; Mesenteries and Related Structures 18200
 Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
- BC Muridae 86375
IT Miscellaneous Descriptors
 HYDROCORTISONE HORMONE-DRUG TRYPTOPHAN PHENYL ALANINE ALANINE CYSTINE
 HYDROXY PROLINE TYROSINE **CITRULLINE** VALINE VALYL ALANINE
 ANTIINFLAMMATORY PERITONEAL FLUID CYTOLOGY
- RN 50-23-7 (HYDROCORTISONE)
51-35-4 (HYDROXY PROLINE)
372-75-8 (**CITRULLINE**)
27493-61-4 (VALYL ALANINE)
56-41-7Q, 6898-94-8Q (ALANINE)
56-89-3Q, 24645-67-8Q (CYSTINE)
60-18-4Q, 55520-40-6Q (TYROSINE)
63-91-2Q, 3617-44-5Q (PHENYL ALANINE)
72-18-4Q, 7004-03-7Q (VALINE)
73-22-3Q, 6912-86-3Q (TRYPTOPHAN)
- L91 ANSWER 38 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1979:137737 BIOSIS
DN BA67:17737
TI **ARGININE** DEIMINASE EC-3.5.3.6 FROM MYCOPLASMA-
ARTHRITIDIS STRUCTURE ACTIVITY RELATIONSHIPS AMONG SUBSTRATES AND COMPETITIVE INHIBITORS.
- AU SMITH D W; GANAWAY R L; FAHRNEY D E
CS DEP. BIOCHEM., COLO. STATE UNIV., FT. COLLINS, COLO. 80523, USA.
SO J BIOL CHEM, (1978) 253 (17), 6016-6020.

CODEN: JBCHA3. ISSN: 0021-9258.

FS BA; OLD

LA English

AB The **arginine** deiminase (L-**arginine** iminohydrolase, EC 3.5.3.6) from *M. arthritidis* catalyzes the irreversible hydrolysis of **arginine** and related guanidine derivatives to NH₃ and the corresponding ureido analog of the substrate. The kinetic constants *K_m*, *k_{cat}* and *k_{cat}/K_m* for the **arginine** deiminase-catalyzed hydrolysis of L-**arginine** are equal to 4 . μ M, 29 s⁻¹, and 7.4 .times. 10⁷ M⁻¹ s⁻¹, respectively, at 25.degree. C and pH 7.2. The enzyme also catalyzes the hydrolysis of L-canavanine, N.alpha.-methyl-L-**arginine**, D-**arginine**, L-**homoarginine**, L-**argininic** acid and guanidine, in order of decreasing 2nd order rate constants (*k_{cat}/K_m*); the 2nd order rate constants from these substrates are 10⁻³-10⁻¹⁰ smaller than the rate constant for L-**arginine**. Twenty-two **arginine** and guanidine analogs were tested for inhibitory capacity. Only 13 are competitive inhibitors having *K_i* [inhibition constant] values in the range 3.2-40 mM. Binding of ligands to the enzyme is apparently dominated by electrostatic or H bonding interactions, or both, of the guanidino and .alpha.-amino group. Neither **citrulline** nor ornithine, the end product of **arginine** degradation in *M. arthritidis*, is an inhibitor of **arginine** deiminase from this organism.

CC Biochemical Methods - Proteins, Peptides and Amino Acids 10054

Biochemical Studies - General 10060

Biochemical Studies - Proteins, Peptides and Amino Acids 10064

Biophysics - General Biophysical Studies 10502

Biophysics - Molecular Properties and Macromolecules 10506

External Effects - Temperature as a Primary Variable 10614

Enzymes - Methods 10804

Enzymes - Chemical and Physical *10806

Enzymes - Physiological Studies *10808

Metabolism - General Metabolism; Metabolic Pathways *13002

Metabolism - Proteins, Peptides and Amino Acids *13012

Temperature: Its Measurement, Effects and Regulation - General Measurement and Methods 23001

Physiology and Biochemistry of Bacteria *31000

Microbiological Apparatus, Methods and Media 32000

BC Mycoplasmataceae 09112

RN 9027-98-9 (**ARGININE** DEIMINASE)

L91 ANSWER 39 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AN 1978:256337 BIOSIS

DN BA66:68834

TI PLASMA AMINO-ACID LEVEL IN **RHEUMATOID ARTHRITIS** AND ANKYLOSING SPONDYLITIS AND ITS VARIATION DURING AGE.

AU PARTSCH G; TAUSCH G; EBERL R

CS LUDWIG-BOLTZMANN-INST. RHEUMATOL. BALNEOL., KURBADSTR. 10, POSTFACH 78, A-1107 WIEN-OBERLAA, AUSTRIA.

SO Z RHEUMATOL, (1978) 37 (3-4), 105-111.

CODEN: ZRHMBQ. ISSN: 0340-1855.

FS BA; OLD

LA English

AB Plasma amino acids [28] of 40 female patients with **rheumatoid arthritis** (RA), 24 male patients with ankylosing spondylitis (ASp) and 19 controls (14 females and 5 males) were investigated. In RA-patients 19 amino acids showed statistically significant differences from healthy people of which 18 were decreased. In ASp-patients 14 amino acid concentrations were statistically altered whereby 10 showed enhanced values. In female RA-patients and controls a linear dependency between distinct amino acids (threonine, glutamic acid, proline, alanine, **citrulline**, tyrosine, phenylalanine, ornithine, lysine and 3-methylhistidine) and advanced age could be demonstrated.

- CC Mathematical Biology and Statistical Methods 04500
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Chordate Body Regions - Back and Buttocks 11310
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Metabolism - Proteins, Peptides and Amino Acids *13012
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology *18006
Gerontology 24500
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
- BC Hominidae 86215
- IT Miscellaneous Descriptors
HUMAN
- L91 ANSWER 40 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1978:254429 BIOSIS
DN BA66:66926
TI CATALYSIS BY **ARGININE** DEIMINASE EC-3.5.3.6 EVIDENCE FOR A COVALENT INTERMEDIATE.
AU SMITH D W; FAHRNEY D E
CS DEP. BIOCHEM., COLO. STATE UNIV., FT. COLLINS, COLO. 80523, USA.
SO BIOCHEM BIOPHYS RES COMMUN, (1978) 83 (1), 101-106.
CODEN: BBRC9. ISSN: 0006-291X.
FS BA; OLD
LA English
AB **Arginine** deiminase (EC 3.5.3.6) [from Mycoplasma **arthritidis**] catalyzes the hydrolysis of **arginine** to NH₃ and **citrulline**. This reaction is postulated to occur in 3 steps: formation of the Michaelis complex, the formation of an amidino-enzyme intermediate and liberation of NH₃ and the rate-determining step, hydrolysis of the amidino-enzyme. The enzymic reaction is accelerated 5-fold by 0.2 M imidazole. This striking effect is expected for the amidino-enzyme mechanism but otherwise is difficult to explain. The putative amidino-enzyme intermediate can be demonstrated by quenching the [¹⁴C]**arginine-arginine** deiminase reaction at low pH. Under these conditions, 0.5 equivalents of ¹⁴C label/mol enzyme dimer were covalently bound.
- CC Radiation - Radiation and Isotope Techniques 06504
Biochemical Methods - Proteins, Peptides and Amino Acids 10054
Biochemical Studies - General 10060
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules 10506
Enzymes - Methods 10804
Enzymes - Chemical and Physical *10806
Enzymes - Physiological Studies *10808
Metabolism - Proteins, Peptides and Amino Acids *13012
Physiology and Biochemistry of Bacteria *31000
Microbiological Apparatus, Methods and Media 32000
- BC Mycoplasmatales 07600
- IT Miscellaneous Descriptors
MYCOPLASMA-ARTHRITIDIS
- RN 9027-98-9 (**ARGININE** DEIMINASE)
- L91 ANSWER 41 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1978:50801 BIOSIS
DN BR14:50801
TI A NEW ANTI NEOPLASTIC AMINO-ACID DERIVATIVE 2 8 DI-N BIS-N BUTYLOXYCARBONYLAMINOMETHYL-L **CITRULLINE** A-924.
AU SAKURAI T; FUJITA H; TOYOSHIMA S
SO Jpn. J. Pharmacol., (1977 (RECD 1978)) 27 (SUPPL), 76P.
CODEN: JJPAZ. ISSN: 0021-5198.
DT Conference

FS BR; OLD
 LA Unavailable
 CC Cytology and Cytochemistry - Animal 02506
 Biochemical Methods - Proteins, Peptides and Amino Acids 10054
 Biochemical Studies - Proteins, Peptides and Amino Acids *10064
 Biophysics - Molecular Properties and Macromolecules *10506
 Pathology, General and Miscellaneous - Therapy 12512
 Digestive System - Pathology *14006
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**
 Pharmacology - General *22002
 Pharmacology - Connective Tissue, Bone and Collagen - Acting Drugs *22012
 Pharmacology - Digestive System *22014
 Neoplasms and Neoplastic Agents - Neoplastic Cell Lines 24005
 Neoplasms and Neoplastic Agents - Therapeutic Agents; Therapy *24008
 Tissue Culture, Apparatus, Methods and Media 32500
 Chemotherapy - General; Methods; Metabolism *38502
 BC Muridae 86375
 IT Miscellaneous Descriptors
 ABSTRACT RAT ASCITES HEPATOMA MOUSE EHRlich CARCINOMA SARCOMA 180
 MITOMYCIN C ANTI NEOPLASTIC-DRUGS
 RN 372-75-8 (**CITRULLINE**)
 1404-00-8 (MITOMYCIN)

 L91 ANSWER 42 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 1976:77061 BIOSIS
 DN BR12:77061
 TI RELATIONSHIP BETWEEN SYSTEMIC AND LIMITED SCLERODERMA.
 AU DOVZHANSKII S I; NIKIFOROVA N E; SLESARENKO N A
 SO Vestn. Dermatol. Venerol., (1976) 1, 60-64.
 CODEN: VDVEAV. ISSN: 0042-4609.
 FS BR; OLD
 LA Unavailable
 CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064
 Pathology, General and Miscellaneous - General *12502
 Metabolism - Proteins, Peptides and Amino Acids 13012
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
***18006**
 Integumentary System - Pathology *18506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology
***34508**
 BC Hominidae 86215
 IT Miscellaneous Descriptors
 HUMAN ORNITHINE **CITRULLINE**
 RN 372-75-8 (**CITRULLINE**)
 70-26-8Q, 7006-33-9Q (ORNITHINE)

=> d his

(FILE 'HOME' ENTERED AT 10:07:58 ON 29 JUN 2003)
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:08:07 ON 29 JUN 2003
 L1 3 S (L-CITRULLINE OR D-CITRULLINE OR DL-CITRULLINE)/CN
 E FIBRIN/CN

FILE 'HCAPLUS' ENTERED AT 10:09:31 ON 29 JUN 2003
 E SSERRE G/AU
 E SERRE G/AU
 L2 45 S E3,E4,E5
 E SEBBAG M/AU
 L3 21 S E3,E4

L4 47 S L2,L3
 E FIBRIN/CT
 E E3+ALL
 L5 842 S E1
 E E2+ALL
 L6 6094 S E5
 L7 17163 S FIBRIN
 E E8+ALL
 L8 15852 S E6,E5+NT
 E FIBRINOGEN
 L9 28056 S E3
 L10 2 S L4 AND L5-L9
 L11 3400 S L1
 L12 6856 S CITRUL?
 L13 12 S L11,L12 AND L4
 L14 2 S L13 AND L10
 L15 11 S (?RHEUMAT? OR ?ARTHRIT?) AND L13,L14
 L16 2 S L14 AND L15
 L17 10 S L10,L13-L15 NOT L16
 L18 2 S L5-L7 AND L11
 L19 5 S L5-L7 AND L12
 L20 9 S L8,L9 AND L11,L12
 L21 9 S L18-L20
 L22 4 S (?RHEUMAT? OR ?ARTHRIT?) AND L21
 L23 4 S L16,L22
 L24 1 S L18,L19 NOT L23
 L25 4 S L21 NOT L22-L24
 SEL DN AN 4
 L26 1 S L25 AND E1-E3
 L27 5 S L23,L26

FILE 'HCAPLUS' ENTERED AT 10:18:55 ON 29 JUN 2003
 SEL RN L16

FILE 'REGISTRY' ENTERED AT 10:19:49 ON 29 JUN 2003

L28 8 S E4-E11
 L29 7 S L28 NOT L1

FILE 'WPIX' ENTERED AT 10:20:23 ON 29 JUN 2003

 E SERRE G/AU
 L30 10 S E3,E4
 E SEBBAG M/AU
 L31 6 S E3,E4
 L32 11 S L30,L31
 L33 453 S ?CITRUL?/BIX
 E CITRULLINE/DCN
 E E3+ALL
 L34 139 S E2 OR 1241/DRN
 L35 1 S E4
 L36 32 S E6
 L37 5 S L32 AND L33-L36
 L38 1 S L37 AND ?FIBRIN?/BIX
 L39 5 S L37,L38
 L40 929 S (C07K014-745 OR C07K014-75 OR A61K038-36)/IC,ICM,ICS,ICA,ICI
 E B04-N02+ALL/MC
 E B04-N0200E+ALL/MC
 L41 2 S L33,L34 AND L40
 L42 11 S L33,L34 AND ?FIBRIN?/BIX
 L43 11 S L41,L42
 L44 1 S L43 AND (A61P019-02 OR A61P029)/IC,ICM,ICS,ICA,ICI
 L45 3 S L43 AND (B14-C06 OR C14-C06 OR B12-D09 OR C12-D09 OR B14-C09?
 L46 3 S L43 AND (P421 OR P423)/M0,M1,M2,M3,M4,M5,M6
 L47 3 S L44-L46

L48 1 S L47 NOT NITROSAT?/TI
L49 8 S L43 NOT L47
SEL DN AN 4 6 8
L50 3 S E1-E9 AND L49
L51 4 S (CIT AND ?FIBRIN?)/BIX
L52 1 S CIT/BIX AND L40
L53 4 S L51,L52
SEL DN AN 3
L54 1 S L53 AND E10-E12
L55 8 S L50,L54,L39 AND L30-L54
L56 6 S L32 NOT L55

FILE 'WPIX' ENTERED AT 10:37:57 ON 29 JUN 2003

FILE 'MEDLINE' ENTERED AT 10:38:19 ON 29 JUN 2003

L57 2022 S L1
L58 907 S CIT
L59 3976 S ?CITRUL?
L60 4805 S L57-L59
E FIBRIN/CT
E E3 ALL
E FIBRIN/CT
E E3+ALL
L61 15242 S E5+NT
L62 8800 S E5/CN
L63 24760 S E5/BI
L64 4 S L60 AND L61-L63
L65 17 S L60 AND ?FIBRIN?
L66 17 S L64,L65
L67 2 S L66 AND (?RHEUMAT? OR ?ARTHRIT?)
E ARTHRITIS/CT
E E3+ALL
L68 2 S L66 AND E4+NT
L69 0 S L66 AND (E41+NT OR E42+NT)
L70 2 S L67,L68

FILE 'MEDLINE' ENTERED AT 10:40:44 ON 29 JUN 2003

FILE 'BIOSIS' ENTERED AT 10:40:59 ON 29 JUN 2003

L71 1729 S L1
L72 1070 S L58
L73 5784 S L59
L74 9 S L71-L73 AND ?FIBRIN?
L75 56 S L73 AND (?RHEUMAT? OR ?ARTHRIT?)
L76 59 S 18006/CC AND L73
L77 2 S L73 AND (SERRE G? OR SEBBAH M?)/AU
L78 21 S 150?/CC AND L75,L76
L79 0 S L74 AND L78
L80 27 S L75,L76 AND (?ARGIN? OR ARG)
L81 48 S L75,L76 NOT L80
L82 10 S FILAG? AND L75,L76
L83 30 S ?ANTIBOD? AND L75,L76
L84 50 S 345?/CC AND L75,L76
L85 47 S L75,L76,L78,L80-L84 AND PY<=2000
L86 0 S L74 AND L85
L87 37 S L85 AND CITRULLINE
L88 0 S L85 AND CIT
L89 10 S L85 NOT L87
SEL DN AN 1-5 L89
L90 5 S L89 AND E1-E10
L91 42 S L87,L90

FILE 'BIOSIS' ENTERED AT 10:47:42 ON 29 JUN 2003

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 10102-43-9 (NITRIC OXIDE)
14797-65-0 (NITRITE)
372-75-8 (**CITRULLINE**)

L91 ANSWER 17 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:470277 BIOSIS
DN PREV199800470277
TI Anti-**citrullinated** peptide **antibodies** in type II mixed
cryoglobulinemia and psoriatic arthropathy.
AU Bordin, Giorgio (1); Gauna, Roberta (1); Schellekens, Gerard A.; Van
Venrooij, Walther J.
CS (1) Dep. Intern. Med. II, Hosp. "Maggiore della Carita", 28100 Novara
Italy
SO Arthritis & Rheumatism, (**Sept.**, 1998) Vol. 41, No. 9 SUPPL., pp.
S349.
Meeting Info.: 62nd National Scientific Meeting of the American College of
Rheumatology and the 33rd National Scientific Meeting of the Association
of Rheumatology Health Professionals San Diego, California, USA November
8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.

DT Conference
LA English
CC Immunology and Immunochemistry - Immunopathology, Tissue Immunology
*34508
Blood, Blood-Forming Organs and Body Fluids - Blood, Lymphatic and
Reticuloendothelial Pathologies *15006
Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology
*18006
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520

BC Hominidae 86215
IT Major Concepts
Rheumatology (Human Medicine, Medical Sciences)
IT Diseases
psoriatic arthropathy: integumentary system disease, joint disease;
type II mixed cryoglobulinemia: blood and lymphatic disease

IT Chemicals & Biochemicals
anti-**citrullinated** peptide **antibodies**

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae)

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L91 ANSWER 18 OF 42 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:468694 BIOSIS
DN PREV199800468694
TI Association between **antibodies** to **citrulline**
-containing peptides in the sera of **rheumatoid arthritis**
(RA) patients and ra-related HLA class II haplotypes.
AU Visser, H. (1); Zanelli, E.; Schellekens, G.; Van Venrooij, W.; Schreuder,
G.; Breedveld, F. C. (1); Hazes, J. M. W.
CS (1) Dep. Rheumatol., Leiden Univ. Med. Centre, Leiden Netherlands
SO Arthritis & Rheumatism, (**Sept.**, 1998) Vol. 41, No. 9 SUPPL., pp.
S84.
Meeting Info.: 62nd National Scientific Meeting of the American College of
Rheumatology and the 33rd National Scientific Meeting of the Association
of Rheumatology Health Professionals San Diego, California, USA November

Human protein: P02675 - Fibrinogen beta chain precursor [Contains: Fibrinopeptide B]. - EMBL Bioinformatic Harvester

EMBL-Heidelberg - Harvester(c) - gfp-cdna - pepperkok-team

Insert-your-question-or-comment-here

feedback

Length: 491 aa, molecular weight: 55928 Da, CRC64 checksum: B92FFB9976AB53C5

claimed
SEQIDNO:2

MKRMVSWSFH	KLKTMKHL	LLL	CVFLVKS	QGVNDNEEGF	FSARGHRPLD	KKREEAPSLR	60
PAPPPISGGG	YRARPAAAA	TQKKVERKAP	DAGGCLHADP	DLGVLCPTGC	QLQEALLQQE		120
RPIRNSVDEL	NNNVEAVSQT	SSSSFQYMYL	LKDLWQKROK	QVKDNENVVN	EYSSELEKHQ		180
LYIDETVNSN	IPTNLRVLRS	ILENLRSKIQ	KLESDVSAQM	EYCRTPCTVS	CNIPVVSGKE		240
CEEIIRKGGE	TSEMYLIQPD	SSVKPYRVYC	DMNTENGGWT	VIQNRQDGSV	DFGRKWDPYK		300
QGFGNVATNT	DGKNYCGLPG	EYWLGN	NDKIS	QLTRMGPT	ELIEMEDWKGD	KVKAHYGGFT	360
VQNEANKYQI	SVNKYRGTAG	NALMDGASQL	MGENRTMTIH	NGMFFSTYDR	DNDGWLTS	DDP	420
RKQCSKEDGG	GWWYNRCHAA	NPNGRYYWGG	QYTWDMAKHG	TDDGVVWMNW	KGSWYSMRKM		480
SMKIRPFFPQ	Q						491

//

GoTo: EBI - Hinxton - "SWALL" database

General information

Entry name FIBB_HUMAN

Accession number P02675

Created Rel. 01, 21-JUL-1986

Sequence update Rel. 26, 1-JUL-1993

Annotation update Rel. 42, 15-SEP-2003

Description and origin of the Protein

Description Fibrinogen beta chain precursor [Contains: Fibrinopeptide B].

Gene name(s) FGB.

Organism source Homo sapiens (Human).

Taxonomy Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

NCBI-TaxID 9606

References

- [1] Chung,D.W., Harris,J.E., Davie,E.W.,
Nucleotide sequences of the three genes coding for human fibrinogen.
(1990) *Adv. Exp. Med. Biol.* 281:39-48

Position SEQUENCE FROM N.A.

Medline 91344740

PubMed 2102623

- [2] Chung,D.W., Que,B.G., Rixon,M.W., Mace,M. Jr., Davie,E.W.,
Characterization of complementary deoxyribonucleic acid and genomic
deoxyribonucleic acid for the beta chain of human fibrinogen.

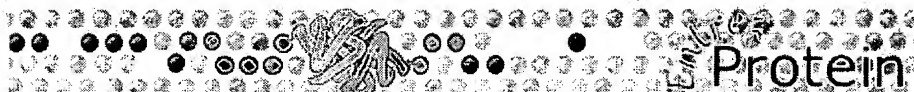
FT	VARSP LIC	631	644	DCDDVLQTHPSGTQ -> GIHTSPLGKPSLSP (in
FT				isoform Alpha).
FT				/FTid=VSP_001531.
FT	VARSP LIC	645	866	Missing (in isoform Alpha).
FT				/FTid=VSP_001532.
FT	VARIANT	6	6	I -> V.
FT				/FTid=VAR_011609.
FT	VARIANT	26	26	D -> N (IN LILLE-1).
FT				/FTid=VAR_002390.
FT	VARIANT	31	31	G -> V (IN ROUEN-1).
FT				/FTid=VAR_002391.
FT	VARIANT	35	35	R -> C (IN MANY VARIANTS).
FT				/FTid=VAR_002392.
FT	VARIANT	35	35	R -> H (IN MANY VARIANTS).
FT				/FTid=VAR_002393.
FT	VARIANT	37	37	P -> L (IN KYOTO-2).
FT				/FTid=VAR_002394.
FT	VARIANT	38	38	R -> N (IN MUNICH-1).
FT				/FTid=VAR_002395.
FT	VARIANT	38	38	R -> S (IN DETROIT-1).
FT				/FTid=VAR_002396.
FT	VARIANT	38	38	R -> G (IN AARHUS-1).
FT				/FTid=VAR_002397.
FT	VARIANT	39	39	V -> D (IN CANTERBURY).
FT				/FTid=VAR_010730.
FT	VARIANT	66	66	S -> T.
FT				/FTid=VAR_002398.
FT	VARIANT	160	160	R -> S (IN LIMA).
FT				/FTid=VAR_002399.
FT	VARIANT	331	331	T -> A (IN dbSNP:6050).
FT				/FTid=VAR_011610.
FT	VARIANT	446	446	K -> E (IN dbSNP:6052).
FT				/FTid=VAR_014168.
FT	VARIANT	453	453	S -> N (IN CARACAS-2).
FT				/FTid=VAR_002400.
FT	VARIANT	456	456	T -> A.
FT				/FTid=VAR_011611.
FT	VARIANT	545	545	E -> V (IN RENAL AMYLOIDOSIS).
FT				/FTid=VAR_010731.
FT	VARIANT	573	573	R -> C (IN DUSART/PARIS-5).
FT				/FTid=VAR_002401.
FT	VARIANT	573	573	R -> L (IN RENAL AMYLOIDOSIS).
FT				/FTid=VAR_010732.
FT	CONFLICT	184	184	C -> W (IN REF. 6).
FT	CONFLICT	215	216	SR -> RS (IN REF. 7).
FT	CONFLICT	299	299	S -> G (IN REF. 7).
FT	CONFLICT	304	304	S -> G (IN REF. 7).
FT	CONFLICT	317	318	GT -> SG (IN REF. 8).
SQ	SEQUENCE	866 AA;	94973 MW;	EA73A81204D8AEC4 CRC64;
	MFSMRIVCLV	LSVVGTAWTA	DSGEGDFLAE	GGGVRGPRVV ERHQSACKDS DWPFCSDEDW
	NYKCPSGCRM	KGLIDEVNQD	FTNRINKLKN	SLFEYQKNNK DSHSLTTNIM EILRGDFSSA
	NNRDNTYNRV	SEDLRSRIEV	LKRKVIEKVQ	HIQLLQKNVR AQLVDMKRLE VDIDIKIRSC
	RGSCSRALAR	EVDLKDIEDQ	QKQLEQVIAK	DLLPSRDRQH LPLIKMKPVP DLVPGNFKFSQ
	LQKVPPPEWKA	LTDMPQMRME	LERPGGNEIT	RGGSTSYGTG SETESPRNPS SAGSWNSGSS
	GPGSTGNRNP	GSSGTGGTAT	WKPGSSGPGS	TGSWNSGSSG TGSTGNQNP
	NPSSSERGSA	GHWTSSESVS	GSTGQWHSES	GSFRPDSPGS GNARPNPNPDW GTFEEVSGNV
	SPGTRREYHT	EKLVTSGDK	ELRTGKEKVT	SGSTTTTTRS CSKTVTKTVI GPDGHKEVTK
	EVVTSEDGSD	CPEAMDGLTL	SGIGTLDGFR	HRHPDEAAFF DTASTGKTFP GFFSPMLGEF
	VSETESRGSE	SGIFTNTKES	SSHHPGIAEF	PSRGKSSSYS KOFTSSTS SYN RGDSTFESKS
	YKMADEAGSE	ADHEGTHSTK	RGHAKSRPVR	DCDDVLQTHP SGTQSGIFNI KLPGSSKIFS
	VYCDQETSLG	GWLLIQQRMD	GSLNFNRTWQ	DYKRGFGSLN DEGEGEFWLG NDYLHLLTQR
	GSVLRVELED	WAGNEAYAEY	HFRVGSEAE	G YALQVSSYEG TAGDALIEGS VEEGAEYTSH
	NNMQFSTFDR	DADQWEENCA	EVYGGGWYN	NCQAANLNGI YYPGGSYDPR NNSPYEIE
	VVWVSFRGAD	YSLRAVRMKI	RPLVTQ	

P02671

SEQ ID No: 1

Fibrinogen 2-chain

//



PubMed

Nucleotide

Protein

Genome

Structure

PMC

Taxonomy

OMIM

Boo

Search for

Limits

Preview/Index

History

Clipboard

Details

1: P02671. Fibrinogen alpha/...[gi:1706799]

BLink, Domains, Links

LOCUS P02671 866 aa linear PRI 01-OCT-1996
 DEFINITION FIBRINOGEN ALPHA AND ALPHA-E CHAIN PRECURSORS.
 ACCESSION P02671
 VERSION P02671 GI:1706799
 DBSOURCE swissprot: locus FIBA_HUMAN, accession P02671;
 class: standard.
 created: Jul 21, 1986.
 sequence updated: Oct 1, 1996.
 annotation updated: Oct 1, 1996.
 xrefs: gi: 458553, gi: 458555, gi: 182406, gi: 182407, gi: 182423,
 gi: 182424, gi: 182425, gi: 182426, gi: 182427, gi: 182428, gi:
 532481, gi: 532482, pdb accession 1BBR
 xrefs (non-sequence databases): SWISS-2DPAGEP02671, MIM 134820
 KEYWORDS BLOOD COAGULATION; PLASMA; PLATELET; PHOSPHORYLATION; SIGNAL;
 3D-STRUCTURE; DISEASE MUTATION; POLYMORPHISM; ALTERNATIVE SPLICING.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
 Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 866)
 AUTHORS Fu, Y., Weissbach, L., Plant, P.W., Oddoux, C., Cao, Y., Liang, T.J.,
 Roy, S.N., Redman, C.M. and Griening, G.
 TITLE Carboxy-terminal-extended variant of the human fibrinogen alpha
 subunit: a novel exon conferring marked homology to beta and gamma
 subunits
 JOURNAL Biochemistry 31 (48), 11968-11972 (1992)
 MEDLINE 93090725
 REMARK SEQUENCE FROM N.A. (ALPHA-E FORM).
 REFERENCE 2 (residues 1 to 866)
 AUTHORS CHUNG, D.W. and GRIENINGER, G.
 JOURNAL (in) EBERT, R.F. (Ed.);
 INDEX OF VARIANT HUMAN FIBRINOGENS: 3-24;
 CRC PRESS, BOCA RATON (1994)
 REMARK SEQUENCE FROM N.A. (ALPHA-E FORM).
 REFERENCE 3 (residues 1 to 866)
 AUTHORS Chung, D.W., Harris, J.E. and Davie, E.W.
 TITLE Nucleotide sequences of the three genes coding for human fibrinogen
 JOURNAL Adv. Exp. Med. Biol. 281, 39-48 (1990)
 MEDLINE 91344740
 REMARK SEQUENCE OF 1-655 FROM N.A. (ALPHA-E FORM).
 TISSUE=LIVER
 REFERENCE 4 (residues 1 to 866)
 AUTHORS Kant, J.A., Lord, S.T. and Crabtree, G.R.
 TITLE Partial mRNA sequences for human A alpha, B beta, and gamma
 fibrinogen chains: evolutionary and functional implications.
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 80 (13), 3953-3957 (1983)
 MEDLINE 83247396
 REMARK SEQUENCE FROM N.A. (ALPHA FORM).

REFERENCE 5 (residues 1 to 866)
AUTHORS Rixon,M.W., Chan,W.Y., Davie,E.W. and Chung,D.W.
TITLE Characterization of a complementary deoxyribonucleic acid coding
for the alpha chain of human fibrinogen
JOURNAL Biochemistry 22 (13), 3237-3244 (1983)
MEDLINE 83283432
REMARK SEQUENCE OF 1-629 FROM N.A.

REFERENCE 6 (residues 1 to 866)
AUTHORS HENSCHEN,A., LOTTSPEICH,F., SOUTHAN,C. and TOPFER-PETERSEN,E.
JOURNAL (in) PROC. 28TH COLLOQ., PEETERS,H. (Ed.);
PROTIDES OF THE BIOLOGICAL FLUIDS: 1-56;
PERGAMON PRESS, OXFORD (1980)
REMARK SEQUENCE OF 20-629.

REFERENCE 7 (residues 1 to 866)
AUTHORS Watt,K.W., Cottrell,B.A., Strong,D.D. and Doolittle,R.F.
TITLE Amino acid sequence studies on the alpha chain of human fibrinogen.
Overlapping sequences providing the complete sequence
JOURNAL Biochemistry 18 (24), 5410-5416 (1979)
MEDLINE 80088231
REMARK SEQUENCE OF 20-629, AND DISULFIDE BONDS.

REFERENCE 8 (residues 1 to 866)
AUTHORS Imam,A.M., Eaton,M.A., Williamson,R. and Humphries,S.
TITLE Isolation and characterisation of cDNA clones for the A alpha- and
gamma-chains of human fibrinogen
JOURNAL Nucleic Acids Res. 11 (21), 7427-7434 (1983)
MEDLINE 84069777
REMARK SEQUENCE OF 110-156 FROM N.A.

REFERENCE 9 (residues 1 to 866)
AUTHORS Chung,D.W., Rixon,M.W., Que,B.G. and Davie,E.W.
TITLE Cloning of fibrinogen genes and their cDNA
JOURNAL Ann. N. Y. Acad. Sci. 408, 449-456 (1983)
MEDLINE 83254384
REMARK SEQUENCE OF 605-644 FROM N.A. (ALPHA FORM).

REFERENCE 10 (residues 1 to 866)
AUTHORS BLOMBACK,B., BLOMBACK,M., GRONDAHL,N.J., GUTHRIE,C. and HINTON,M.
JOURNAL ACTA CHEM. SCAND. 19, 1788-1789 (1965)
REMARK SEQUENCE OF 20-35.

REFERENCE 11 (residues 1 to 866)
AUTHORS Cottrell,B.A., Strong,D.D., Watt,K.W. and Doolittle,R.F.
TITLE Amino acid sequence studies on the alpha chain of human fibrinogen.
Exact location of cross-linking acceptor sites
JOURNAL Biochemistry 18 (24), 5405-5410 (1979)
MEDLINE 80088230
REMARK CROSS-LINKING ACCEPTOR SITES.

REFERENCE 12 (residues 1 to 866)
AUTHORS Fretto,L.J., Ferguson,E.W., Steinman,H.M. and McKee,P.A.
TITLE Localization of the alpha-chain cross-link acceptor sites of human
fibrin
JOURNAL J. Biol. Chem. 253 (7), 2184-2195 (1978)
MEDLINE 78130085
REMARK CROSS-LINKING ACCEPTOR SITES.

REFERENCE 13 (residues 1 to 866)
AUTHORS Blomback,B., Hessel,B. and Hogg,D.
TITLE Disulfide bridges in nh2 -terminal part of human fibrinogen
JOURNAL Thromb. Res. 8 (5), 639-658 (1976)
MEDLINE 76225080
REMARK VARIANT, AND DISULFIDE BONDS.

REFERENCE 14 (residues 1 to 866)
AUTHORS Doolittle,R.F.
TITLE Fibrinogen and fibrin

JOURNAL Annu. Rev. Biochem. 53, 195-229 (1984)
MEDLINE 84305751
REMARK REVIEW, EM STRUCTURE, POLYMERIZATION, AND LIGANDS.
REFERENCE 15 (residues 1 to 866)
AUTHORS Kimura,S. and Aoki,N.
TITLE Cross-linking site in fibrinogen for alpha 2-plasmin inhibitor
JOURNAL J. Biol. Chem. 261 (33), 15591-15595 (1986)
MEDLINE 87057190
REMARK CROSS-LINKING SITE FOR ALPHA-2-PLASMIN INHIBITOR.
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AUTHORS Itarte,E., Plana,M., Guasch,M.D. and Martos,C.
TITLE Phosphorylation of fibrinogen by casein kinase 1
JOURNAL Biochem. Biophys. Res. Commun. 117 (2), 631-636 (1983)
MEDLINE 84104274
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TITLE The structure of residues 7-16 of the A alpha-chain of human
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JOURNAL J. Biol. Chem. 267 (11), 7911-7920 (1992)
MEDLINE 92218459
REMARK X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS) OF 26-39.
REFERENCE 18 (residues 1 to 866)
AUTHORS Yoshida,N., Okuma,M., Hirata,H., Matsuda,M., Yamazumi,K. and
Asakura,S.
TITLE Fibrinogen Kyoto II, a new congenitally abnormal molecule,
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JOURNAL Blood 78 (1), 149-153 (1991)
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PEREZ-REQUEJO,J.L. and MATSUDA,M.
TITLE Fibrinogen Lima: a homozygous dysfibrinogen with an A
alpha-arginine-141 to serine substitution associated with extra
N-glycosylation at A alpha-asparagine-139. Impaired fibrin gel
formation but normal fibrin-facilitated plasminogen activation
catalyzed by tissue-type plasminogen activator
JOURNAL J. Clin. Invest. 90 (1), 67-76 (1992)
MEDLINE 92340680
REMARK VARIANT LIMA.
REFERENCE 20 (residues 1 to 866)
AUTHORS MAEKAWA,H., YAMAZUMI,K., MURAMATSU,S., KANEKO,M., HIRATA,H.,
TAKAHASHI,N., DE BOSCH,N.B., CARVAJAL,Z., OJEDA,A.,
AROCHE-PINANGO,C.L. and MATSUDA,M.
TITLE An A alpha Ser-434 to N-glycosylated Asn substitution in a
dysfibrinogen, fibrinogen Caracas II, characterized by impaired
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JOURNAL J. Biol. Chem. 266 (18), 11575-11581 (1991)
MEDLINE 91268018
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AUTHORS KOOPMAN,J., HAVERKATE,F., GRIMBERGEN,J., LORD,S.T., MOSESSON,M.W.,
DIORIO,J.P., SIEBENLIST,K.S., LEGRAND,C., SORIA,J., SORIA,C. and
CAEN,J.P.
TITLE Molecular basis for fibrinogen Dusart (A alpha 554 Arg-->Cys) and
its association with abnormal fibrin polymerization and
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JOURNAL J. Clin. Invest. 91 (4), 1637-1643 (1993)
 MEDLINE 93232289
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 CONVERSION OF FIBRINOGEN TO FIBRIN IS TRIGGERED BY THROMBIN, WHICH
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 [SUBUNIT] HEXAMER CONTAINING 2 SETS OF 3 NONIDENTICAL CHAINS
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 DIVERGING FROM THIS NODULE ARE 2 THREE-CHAIN COILED COILS, WHICH
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 [PTM] ABOUT ONE-THIRD OF THE ALPHA CHAINS IN THE MOLECULES IN BLOOD
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 [ALTERNATIVE PRODUCTS] TWO DIFFERENT FORMS ARE PRODUCED BY
 ALTERNATIVE SPLICING. THE ALPHA FORM IS THE PREDOMINANT FORM. THE
 FORM SHOWN IS ALPHA-E.

FEATURES	Location/Qualifiers
<u>source</u>	1..866 /organism="Homo sapiens" /db_xref="taxon:9606"
<u>gene</u>	1..866 /gene="FGA"
<u>Protein</u>	1..866 /gene="FGA"
<u>Region</u>	/product="FIBRINOGEN ALPHA AND ALPHA-E CHAIN PRECURSORS" 1..19 /gene="FGA" /region_name="Signal"
<u>Region</u>	20..35 /gene="FGA" /region_name="Processed active peptide" /note="FIBRINOPEPTIDE A."
<u>Site</u>	22 /gene="FGA" /site_type="phosphorylation"
<u>Region</u>	26 /gene="FGA" /region_name="Variant" /note="D -> N (IN LILLE-1)."
<u>Region</u>	31 /gene="FGA" /region_name="Variant" /note="G -> V (IN ROUEN-1)."
<u>Site</u>	35..36 /gene="FGA"

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/note="CLEAVAGE (BY THROMBIN; RELEASE FIBRINOPEPTIDE A)."
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/gene="FGA"
/region_name="Variant"
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Region 35
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/region_name="Variant"
/note="R -> H (IN MANY VARIANTS)."
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/gene="FGA"
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/note="FIBRINOGEN ALPHA-E CHAIN."
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OF THE GAMMA CHAIN OF ANOTHER FIBRIN MONOMER."
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/region_name="Variant"
/note="R -> N (IN MUNICH-1)."
Region 38
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/region_name="Variant"
/note="R -> S (IN DETROIT-1)."
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/bond_type="disulfide"
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Bond bond(68)
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/bond_type="disulfide"
/note="INTERCHAIN (WITH C-106 IN BETA)."
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/region_name="Variant"
/note="R -> S (IN LIMA)."
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/bond_type="disulfide"
/note="INTERCHAIN (WITH C-165 IN GAMMA)."
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/gene="FGA"
/region_name="Conflict"
/note="C -> W (IN REF. 5)."
Bond bond(184)
/gene="FGA"
/bond_type="disulfide"
/note="INTERCHAIN (WITH C-223 IN BETA)."
Region 215..216
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Region 299
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Region 304
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/note="S -> G (IN REF. 6)."
Region 317..318
/gene="FGA"
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/note="CROSS-LINKS TO ALPHA-2-PLASMIN INHIBITOR."
Region 331
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Site 385
/gene="FGA"
/site_type="unclassified"
/note="ACCEPTOR SITE FOR CROSS-LINKING."
Region 453
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Site 453
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/bond_type="disulfide"
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/region_name="Variant"
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Region 631..644
/gene="FGA"

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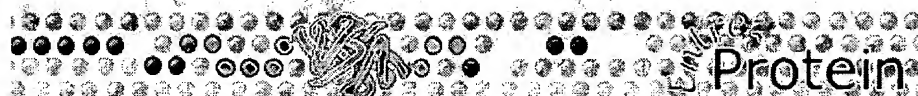
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181 rgscsralar evdlkdyedq qkqlaqviak dllpsrdrqh lplikmkpvp dlvpgnfksq  
241 lqkvppewka ltdmpqmrme lerpggneit rggstsygtg setesprnps sagswnsgss  
301 gpgstgnrnp gssgtggtat wkpqssgpgs tgswnsgssg tgstgnqnpq sprpgstgtw  
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481 evvtsedgsd cpeamdltl sgigtldgfr hrhpdeaaaff dtastgktfp gffspmlgef  
541 vsetesrgse sgiftntkes sshhpgiaef psrgksssys kqftsstsyn rgdstfesks  
601 ykmadeagse adhegthstk rghaksrpvr dcddvlqthp sgtqsgifni klpqsskifs  
661 vycdqetslg gwlliqqrmd gslnfnrtwq dykrqfgsln degegefwwg ndylhlhtqr  
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841 vwwvsfrgad yslravrmki rplvtq
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//

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Jul 17 2003 11:56:53



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Nucleotide

Protein

Genome

Structure

PMC

Taxonomy

OMIM

Bio

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Show: ☐ 1: P02671. Fibrinogen alpha/...[gi:1706799]

BLink, Domains, Links

LOCUS P02671 866 aa linear PRI 01-OCT-1996
 DEFINITION FIBRINOGEN ALPHA AND ALPHA-E CHAIN PRECURSORS.
 ACCESSION P02671
 VERSION P02671 GI:1706799
 DBSOURCE swissprot: locus FIBA_HUMAN, accession P02671;
 class: standard.
 created: Jul 21, 1986.
 sequence updated: Oct 1, 1996.
 annotation updated: Oct 1, 1996.
 xrefs: gi: 458553, gi: 458555, gi: 182406, gi: 182407, gi: 182423,
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 532481, gi: 532482, pdb accession 1BBR
 xrefs (non-sequence databases): SWISS-2DPAGEP02671, MIM 134820
 KEYWORDS BLOOD COAGULATION; PLASMA; PLATELET; PHOSPHORYLATION; SIGNAL;
 3D-STRUCTURE; DISEASE MUTATION; POLYMORPHISM; ALTERNATIVE SPLICING.
 SOURCE Homo sapiens (human)
 ORGANISM Homo sapiens
 Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
 Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (residues 1 to 866)
 AUTHORS Fu, Y., Weissbach, L., Plant, P.W., Oddoux, C., Cao, Y., Liang, T.J.,
 Roy, S.N., Redman, C.M. and Griening, G.
 TITLE Carboxy-terminal-extended variant of the human fibrinogen alpha
 subunit: a novel exon conferring marked homology to beta and gamma
 subunits
 JOURNAL Biochemistry 31 (48), 11968-11972 (1992)
 MEDLINE 93090725
 REMARK SEQUENCE FROM N.A. (ALPHA-E FORM).
 REFERENCE 2 (residues 1 to 866)
 AUTHORS CHUNG, D.W. and GRIENINGER, G.
 JOURNAL (in) EBERT, R.F. (Ed.);
 INDEX OF VARIANT HUMAN FIBRINOGENS: 3-24;
 CRC PRESS, BOCA RATON (1994)
 REMARK SEQUENCE FROM N.A. (ALPHA-E FORM).
 REFERENCE 3 (residues 1 to 866)
 AUTHORS Chung, D.W., Harris, J.E. and Davie, E.W.
 TITLE Nucleotide sequences of the three genes coding for human fibrinogen
 JOURNAL Adv. Exp. Med. Biol. 281, 39-48 (1990)
 MEDLINE 91344740
 REMARK SEQUENCE OF 1-655 FROM N.A. (ALPHA-E FORM).
 TISSUE=LIVER
 REFERENCE 4 (residues 1 to 866)
 AUTHORS Kant, J.A., Lord, S.T. and Crabtree, G.R.
 TITLE Partial mRNA sequences for human A alpha, B beta, and gamma
 fibrinogen chains: evolutionary and functional implications
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 80 (13), 3953-3957 (1983)
 MEDLINE 83247396
 REMARK SEQUENCE FROM N.A. (ALPHA FORM).

REFERENCE 5 (residues 1 to 866)
AUTHORS Rixon,M.W., Chan,W.Y., Davie,E.W. and Chung,D.W.
TITLE Characterization of a complementary deoxyribonucleic acid coding
for the alpha chain of human fibrinogen
JOURNAL Biochemistry 22 (13), 3237-3244 (1983)
MEDLINE 83283432
REMARK SEQUENCE OF 1-629 FROM N.A.

REFERENCE 6 (residues 1 to 866)
AUTHORS HENSCHEN,A., LOTTSPEICH,F., SOUTHAN,C. and TOPFER-PETERSEN,E.
JOURNAL (in) PROC. 28TH COLLOQ., PEETERS,H. (Ed.);
PROTIDES OF THE BIOLOGICAL FLUIDS: 1-56;
PERGAMON PRESS, OXFORD (1980)
REMARK SEQUENCE OF 20-629.

REFERENCE 7 (residues 1 to 866)
AUTHORS Watt,K.W., Cottrell,B.A., Strong,D.D. and Doolittle,R.F.
TITLE Amino acid sequence studies on the alpha chain of human fibrinogen.
Overlapping sequences providing the complete sequence
JOURNAL Biochemistry 18 (24), 5410-5416 (1979)
MEDLINE 80088231
REMARK SEQUENCE OF 20-629, AND DISULFIDE BONDS.

REFERENCE 8 (residues 1 to 866)
AUTHORS Imam,A.M., Eaton,M.A., Williamson,R. and Humphries,S.
TITLE Isolation and characterisation of cDNA clones for the A alpha- and
gamma-chains of human fibrinogen
JOURNAL Nucleic Acids Res. 11 (21), 7427-7434 (1983)
MEDLINE 84069777
REMARK SEQUENCE OF 110-156 FROM N.A.

REFERENCE 9 (residues 1 to 866)
AUTHORS Chung,D.W., Rixon,M.W., Que,B.G. and Davie,E.W.
TITLE Cloning of fibrinogen genes and their cDNA
JOURNAL Ann. N. Y. Acad. Sci. 408, 449-456 (1983)
MEDLINE 83254384
REMARK SEQUENCE OF 605-644 FROM N.A. (ALPHA FORM).

REFERENCE 10 (residues 1 to 866)
AUTHORS BLOMBACK,B., BLOMBACK,M., GRONDAHL,N.J., GUTHRIE,C. and HINTON,M.
JOURNAL ACTA CHEM. SCAND. 19, 1788-1789 (1965)
REMARK SEQUENCE OF 20-35.

REFERENCE 11 (residues 1 to 866)
AUTHORS Cottrell,B.A., Strong,D.D., Watt,K.W. and Doolittle,R.F.
TITLE Amino acid sequence studies on the alpha chain of human fibrinogen.
Exact location of cross-linking acceptor sites
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 [DISEASE] VARIATIONS IN POSITION ARG-35 (THE SITE OF CLEAVAGE OF FIBRINOPEPTIDE A BY THROMBIN) LEADS TO ALPHA-DYSFIBROGENEMIAS.
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source	1..866 /organism="Homo sapiens" /db_xref="taxon:9606"
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Protein	1..866 /gene="FGA" /product="FIBRINOGEN ALPHA AND ALPHA-E CHAIN PRECURSORS"
Region	1..19 /gene="FGA" /region_name="Signal"
Region	20..35 /gene="FGA" /region_name="Processed active peptide" /note="FIBRINOPEPTIDE A."
Site	22 /gene="FGA" /site_type="phosphorylation"
Region	26 /gene="FGA" /region_name="Variant" /note="D -> N (IN LILLE-1)."
Region	31 /gene="FGA" /region_name="Variant" /note="G -> V (IN ROUEN-1)."
Site	35..36 /gene="FGA"

Region /site_type="cleavage"
/note="CLEAVAGE (BY THROMBIN; RELEASE FIBRINOPEPTIDE A)."
35
/gene="FGA"
/region_name="Variant"
/note="R -> C (IN MANY VARIANTS)."
Region 35
/gene="FGA"
/region_name="Variant"
/note="R -> H (IN MANY VARIANTS)."
Region 36..866
/gene="FGA"
/region_name="Mature chain"
/note="FIBRINOGEN ALPHA-E CHAIN."
Site 36..38
/gene="FGA"
/site_type="unclassified"
/note="POLYMERIZATION SITE, BINDING TO THE DISTAL DOMAIN
OF THE GAMMA CHAIN OF ANOTHER FIBRIN MONOMER."
Region 37
/gene="FGA"
/region_name="Variant"
/note="P -> L (IN KYTO-2)."
Region 38
/gene="FGA"
/region_name="Variant"
/note="R -> N (IN MUNICH-1)."
Region 38
/gene="FGA"
/region_name="Variant"
/note="R -> S (IN DETROIT-1)."
Region 38
/gene="FGA"
/region_name="Variant"
/note="R -> G (IN AARHUS-1)."
Bond bond(47)
/gene="FGA"
/bond_type="disulfide"
/note="INTERCHAIN (WITH C-47')."
Bond bond(55)
/gene="FGA"
/bond_type="disulfide"
/note="INTERCHAIN (WITH C-95 IN BETA)."
Bond bond(64)
/gene="FGA"
/bond_type="disulfide"
/note="INTERCHAIN (WITH C-49 IN GAMMA)."
Region 66
/gene="FGA"
/region_name="Variant"
/note="S -> T."
Bond bond(68)
/gene="FGA"
/bond_type="disulfide"
/note="INTERCHAIN (WITH C-106 IN BETA)."
Region 160
/gene="FGA"
/region_name="Variant"
/note="R -> S (IN LIMA)."
Bond bond(180)

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/ gene="FGA"
/ bond_type="disulfide"
/ note="INTERCHAIN (WITH C-165 IN GAMMA)."
Region 184
/ gene="FGA"
/ region_name="Conflict"
/ note="C -> W (IN REF. 5)."
Bond bond(184)
/ gene="FGA"
/ bond_type="disulfide"
/ note="INTERCHAIN (WITH C-223 IN BETA)."
Region 215..216
/ gene="FGA"
/ region_name="Conflict"
/ note="SR -> RS (IN REF. 6)."
Region 299
/ gene="FGA"
/ region_name="Conflict"
/ note="S -> G (IN REF. 6)."
Region 304
/ gene="FGA"
/ region_name="Conflict"
/ note="S -> G (IN REF. 6)."
Region 317..318
/ gene="FGA"
/ region_name="Conflict"
/ note="GT -> SG (IN REF. 7)."
Site 322
/ gene="FGA"
/ site_type="unclassified"
/ note="CROSS-LINKS TO ALPHA-2-PLASMIN INHIBITOR."
Region 331
/ gene="FGA"
/ region_name="Conflict"
/ note="T -> A (IN REF. 6)."
Site 347
/ gene="FGA"
/ site_type="unclassified"
/ note="ACCEPTOR SITE FOR CROSS-LINKING."
Site 385
/ gene="FGA"
/ site_type="unclassified"
/ note="ACCEPTOR SITE FOR CROSS-LINKING."
Region 453
/ gene="FGA"
/ region_name="Variant"
/ note="S -> N (IN CARACAS-2)."
Site 453
/ gene="FGA"
/ site_type="glycosylation"
/ note="IN VARIANT CARACAS-2."
Bond bond(461,491)
/ gene="FGA"
/ bond_type="disulfide"
Region 573
/ gene="FGA"
/ region_name="Variant"
/ note="R -> C (IN DUSART/PARIS-5)."
Region 631..644
/ gene="FGA"

```

Region

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/region_name="Splicing variant"  
/note="DCDDVLQTHPSGTQ -> GIHTSPLGKPSLSP (IN ALPHA FORM)."  
645..866  
/gene="FGA"  
/region_name="Splicing variant"  
/note="MISSING (IN ALPHA FORM)."
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ORIGIN

```
1 mfsmrivclv lsvvgtawta dsgegdfiae gggvrgprvv erhqsackds dwpfcsdedw  
61 nykcpsgcrm kglidevnqd ftnrinklkn slfeyqknnk dshslttnim eilrgdfssa  
121 nnrdntynrv sedlrsriev lkrkviekvq hiqlqknvr aqlvdmkrle vdidikirsc  
181 rgscsralar evdlkdyedq qkqlqeviak dllpsrdrqh lplikmkpvp dlvpgnfksq  
241 lqkvppewka ltdmpqmrme lerpggneit rggstsygtg setesprnps sagswnsgss  
301 gpgstgnrnp gssgtggtat wkpgssgpgs tgswnsgssg tgstgnqnpq sprpgstgtw  
361 npgssergsa ghwtseessvs gstgqwhses gsfrpdspgs gnarpnnpdw gtfeevsgnv  
421 spgtrreyht eklvtstkqdk elrtgkekvt sgsttttrrs csktvtktvi gpdghkevtk  
481 evvtsedgsd cpeamdltl sgigtldgfr hrhpdeaaff dtastgktfp gffspmlgef  
541 vsetesrgse sgiftntkes sshhpgiaef psrgksssys kqftsstsyn rgdstfesks  
601 ykmadeagse adhegthstk rghaksrpvr dcddvlqthp sgtqsgifni klpgsskifs  
661 vycdgetsig gwlliqqrm d gslnftrtwq dykrfgsln degegefwwg ndylhlitqr  
721 gsvlrveled wagneayaey hfrvgseaeg yalqvssyeg tagdalieng veegaeytsh  
781 nnmqfstfdr dadqweenca evygggwwyn ncqaanlngi yypggsydpn nnspeyeng  
841 vvvvsfrgad yslravrmki rplvtq
```

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